BIOMECHANICAL INVESTIGATIONS OF ENDOGRAFTS FOR ABDOMINAL AORTIC ANEURYSM REPAIR

Thesis submitted in accordance with the requirements of

Faculty of Medicine at the University of Liverpool

for the degree of

Doctor of Medicine

By

SAMUEL SHUNAN ZHOU

MBBS, MRCSEd, MRCS Glasg

Regional Vascular Unit

Royal Liverpool University Hospital

Liverpool, L7 8XP, UK

&

Department of Clinical Engineering

University of Liverpool, L69 3GA, UK

October 2009.

Dedicated to

Zongshan Zhou, my mother

Dr Rosemary L. H. Fieldsend, my wife

&

In memory of

Yuegui Zhou, my father

Dr Gerald Arthur Fieldsend and Mrs Edith Helen Fieldsend, my parents-in-law.

ABSTRACT

Introduction

The aim of endovascular aortic aneurysm repair (EVAR), is to isolate the aneurysm sac from the rest of the blood circulation and thereby eliminate the risk of aneurysm rupture. Proximal Type I endoleak and endovascular stent-graft migration are the two commonest causes for failure of the procedure; leading to aneurysm re-pressurisation, and rupture.

Aim

The aims of this research were to examine the relationship between migration and stent-graft oversizing of the proximal aortic neck; the mode of stent-graft migration; to compare the proximal fixation strength between standard and fenestrated stent-graft; to examine the relationship between oversizing and aortic neck length for a proximal seal in standard and fenestrated EVAR; and finally, to measure the longitudinal haemodynamic force (LF) acting on the bifurcated stent-graft in EVAR.

Method

The bench top experimental model for the measurement of proximal displacement force (the force required to displace the stent-graft) comprised a proximal portion of

standard or fenestrated Zenith stent-graft (Cook Europe, Bjaeverskov, Denmark), which was deployed into a prepared, pressurised bovine aorta, a linear drive and a calibrated digital force gauge. Force was applied to the stent-graft and measured with the force gauge. The mode of migration was observed. To investigate the proximal seal in different aortic neck lengths, a sealed proximal portion of standard or fenestrated stent-graft was deployed into the prepared bovine aorta and then placed into a pulsatile circulating system. Under human physiological flow conditions, the leak between the aorta and the stent-graft was observed at different aortic "neck" lengths. In the experiment of measurement of longitudinal haemodynamic force acting on the stent-graft in EVAR, a bifurcated stent-graft model was machined and bonded with a strain gauge. The model was placed into the same pulsatile flow system under human physiological conditions, and the force was measured.

Results

The results of forces required to cause stent-graft migration by 5 mm have revealed that the maximal force is reached at oversizing by 20% in stent-graft with barbs and 30% without barbs. The barbs increase the overall proximal fixation strength. The mode of migration was observed in two phases. Phase one is due to the barbs embedding into the aortic wall, with migration limited to a few millimetres, and it only requires relatively small forces. Phase two occurs when the full fixation strength of the device has been exceeded. The fenestrated stent-graft configuration confers greater proximal fixation strength than conventional devices.

The proximal seal in fenestrated and standard stent-graft was observed, and it was found that the optimal oversize is inversely related to seal zone length. For fenestrated EVAR with bare stent, a seal can be achieved at aortic neck length as short as 5 mm.The results of the measurement of the longitudinal haemodynamic force acting on a bifurcated stent-graft model revealed that the force is strongly dependent on pressure. The fluid viscosity, momentum and pulsatility contribute between 6 and 18% of the total LF. These results confirm that under certain conditions, LF can exceed the fixation strength of some of the current endovascular stent-grafts.

Conclusion

Adequate oversizing improves the proximal fixation strength. Barbs also increase the proximal fixation strength. The mode of stent-graft migration occurs in two stages. The fenestrated stent-graft configuration confers greater proximal fixation strength than conventional devices. The optimal oversize in both fenestrated and standard stent-graft is inversely related to seal zone length. For fenestrated EVAR with bare stent, a seal can be achieved at aortic neck length as short as 5 mm. The longitudinal haemodynamic force acting on a bifurcated stent-graft model is strongly dependent on pressure, and it can exceed the fixation force in some of the current endovascular stent-grafts.

ACKNOWLEDGMENTS

The author wishes to express his thanks to the following:

Dr T. V. How. Senior Lecturer, Department of Clinical Engineering, University of Liverpool, who supervised me. He has been the greatest supporter and advisor. He has taught me the process of scientific investigation and helped me in constructing a scientific paper. He has reviewed my thesis and made extremely valuable contributions.

Dr R. McWilliams. Consultant Interventional Radiologist to the Royal Liverpool University Hospital, who supervised me, helped me conduct the experiment under fluoroscopy, gave me advice in experimental design, and reviewed my thesis.

Mr J. A. Brennan. Consultant Vascular Surgeon to the Royal Liverpool University Hospital, who supervised me and reviewed the draft of my scientific paper. He gave me further advice on my experimental designs. He has been very understanding and a great supporter.

Mr S. R. Vallabhaneni. Consultant Vascular Surgeon to the Royal Liverpool University Hospital, who inspired me with his commitment, hard work and his achievement. He

has set a good example for dedication to his career. He has also helped with construction of a scientific paper.

Professor P. L. Harris. Professor and Consultant Vascular Surgeon to the Royal Liverpool University Hospital, who has supervised me and helped me in construction of abstracts and presentation slides for scientific meetings. He has also given me advice and practical help in my research. He has been my greatest source of inspiration.

Mr G. L. Gilling-Smith. Consultant Vascular Surgeon to the Royal Liverpool University Hospital, who has greatly supported me and encouraged me in my abstracts and presentations for scientific meetings.

Mr J. Blackhurst. Technician, who constructed all the models for my research.

LIST OF CONTENTS

ABBREVIATIONS

AAA	abdominal aortic aneurysm
CT	Computed tomography
DREAM trial	Dutch Randomized Endovascular Aneurysm Management Trial
EUROSTAR	The European Collaborators on Stent Graft Techniques for Abdominal Aortic Aneurysm Repair Registry
EVAR	Endovascular abdominal aortic aneurysm repair
FDF	final displacement force
f_x	longitudinal force
IDF	as initial displacement force
ITT	intention-to-treat
m-DF	mean displacement force
MRI	Magnetic resonance imaging
N	Newton
NICE	the National Institute for Health and Clinical Excellence in UK
OR	open repair abdominal aortic aneurysm
RCTs	randomised controlled trials
RETA	The UK Registry for Endovascular Treatment of Aneurysms
SD	standard deviation
UK EVAR Trial	United Kingdom endovascular abdominal aortic aneurysm repair trial

CHAPTER 1

ABDOMINAL AORTIC ANEURYSM AND CONVENTIONAL MANAGEMENT

1.1 Aneurysm

A true aneurysm is described as a pathological, dilatation of a segment of a blood vessel, (which can be an artery, vein, or lymphatic duct); caused by a congenital or acquired weakness. It involves all three layers of aortic wall (tunica adventitia, tunica media, and tunica intima).

On the other hand, a false aneurysm involves disruption of the intimal and medial layers, with the dilatation lined by adventitia and sometimes by a perivascular clot (Dzau et al 1991), or surrounding tissues.

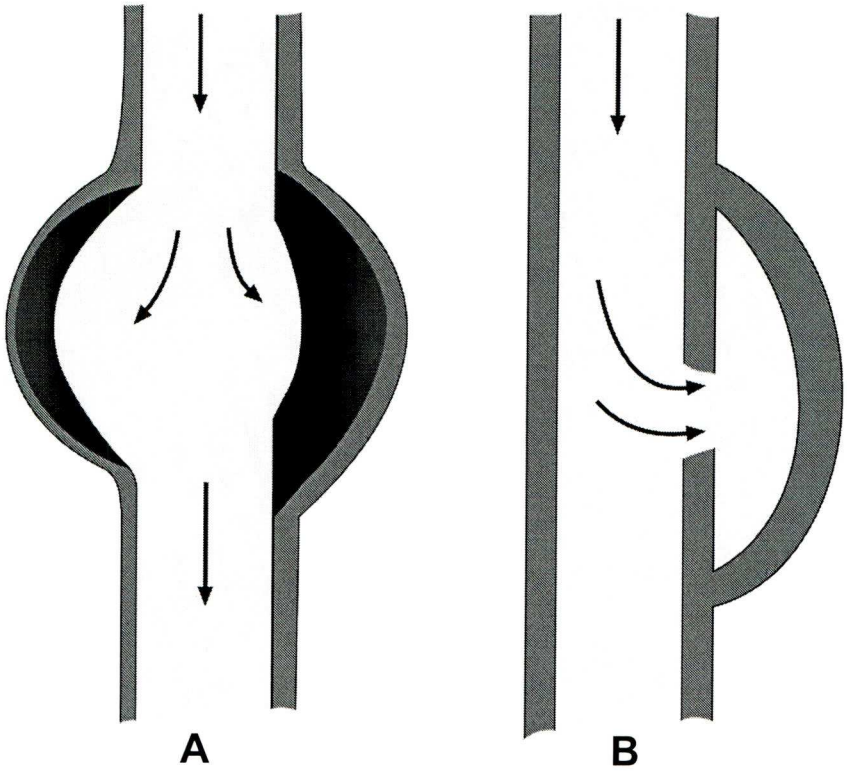

Figure 1.1: Diagram of true aneurysm (A) and false aneurysm (B).
Aneurysm can occur in any part of the human body; however the infrarenal aorta is one of the commonest sites (this diagram is kindly provided by the department of medical illustration, Aberdeen Royal Infirmary, UK).

Despite many established standards, a consensus definition of abdominal aortic aneurysm (AAA) does not exist (Verloes et al 1995). Normal abdominal aortic diameters have been studied previously. In studies of anatomical specimens, the diameter of the inferior aspect of the normal abdominal aorta was less than 15 mm. Radiological studies have found the diameter of the normal abdominal aorta to measure, on average, 19 mm (Williams et al 1989). An increase in diameter of 50% is one accepted criterion for defining an abdominal aortic aneurysm (Appleberg et al, 1994). Other definitions include an infrarenal aorta measurement of 30 mm or more (Yochum et al 1996; Holdsworth et al 1994; Verloes et al 1995) or a ratio of infrarenal to suprarenal diameter greater than 1.5:1 (Verloes et al 1995).

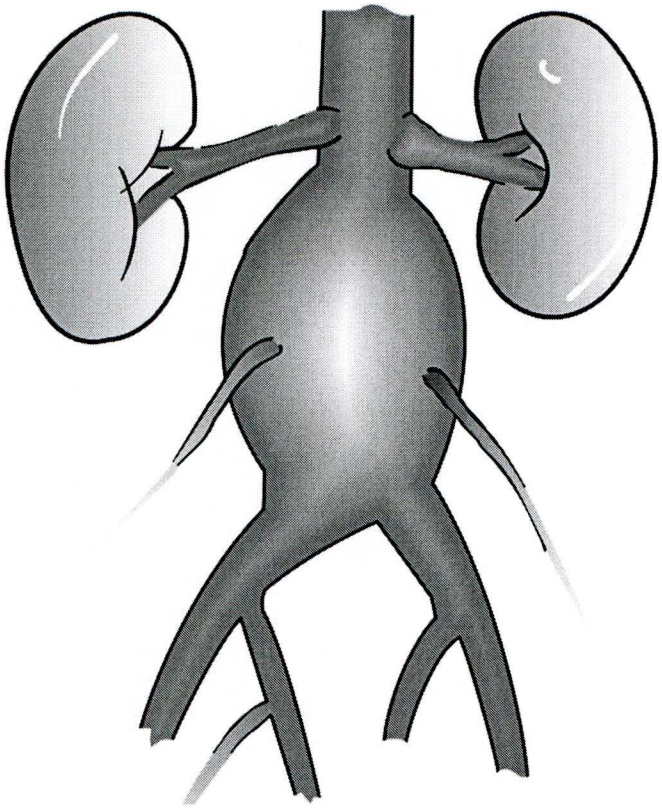

Figure 1.2: A diagram of infrarenal abdominal aortic (kindly provided by the department of medical illustration, Aberdeen Royal Infirmary).

1.2 Prevalence and Incidence of Abdominal Aortic Aneurysm

Aortic aneurysm is a common disease in the Western World. It mainly affects the elderly population. The commonest site for aortic aneurysm is in the abdominal segment, especially infrarenal.

1.2.1 Prevalence

Estimates of the prevalence of AAA can be obtained from population screening surveys and autopsy studies. The prevalence of screen-detected aneurysm in men in England varies between 1.3% and 12.7% (Collin et al 1988; Lucarotti et al1993; Smith et al 1993; Scott et al 1995) depending on the age group screened and the criteria used for the definition of AAA.

A generally accepted definition of a small AAA is an aorta with a diameter from 30 mm to 54mm (Scott et al 1991; Lucarotti et al 1993; Smith et al 1993; Morris et al 1994; Vander Vliet et al 1997). The prevalence defined by an infrarenal aortic diameter ≥ 30mm based on using ultrasound imaging, varied between 4.5% and 8% in men aged between 60 and 80 years (Boll et al 1998; Ashton et al 2001). Whilst the prevalence of AAA greater than 4.0 cm in diameter in men aged between 65 and 75 years is approximately 3% (Crawford et al 2003). Other studies have estimated the prevalence of unsuspected AAA to be 5.4% (Collin et al 1988). Studies have reported prevalence rates of 12% to 33% in first-degree relatives (Appleberg et al 1994; Verloes et al 1995). Increased awareness of abdominal aortic aneurysms, screening programs, and the ageing population are also having contributed to an increase in the incidence of asymptomatic AAA's.

1.2.2 Incidence

Reported incidences of asymptomatic AAA in the literature vary between 3·0 and 117·2 per 100 000 person-years (Melton et al 1984; Castleden et al 1985; Fowkes et al 1989; Pleumeekers et al 1994). All studies report sharp rises in the age-adjusted incidence of AAA in recent years. The average increase in incidence ranges from 4·2% per year in Australia to 11% per year in a report from Rochester, Minnesota, USA. A nationwide study from Denmark reported an increase in the incidence of asymptomatic aneurysm from 7·1 per 100 000 to 25·8 per 100 000 person-years from 1977 to 1990 (Eickhoff et al 1993). This increase was constant over all age groups examined.

The reported incidence of ruptured AAA varies from 1 to 21 per 100,000 person-years (Castleden et al 1985; Ingoldby et al 1986; Mealy et al 1988; Thomas et al 1988; Budd et al 1989; Drott et al 1992). The Goteborg study (Drott et al 1992) found a sevenfold rise in incidence over a period of 36 years. In the UK, the high incidence of AAA was confirmed by the UK small aneurysm trial. Ultrasonic screening studies of the general population show that 1.5% - 3% of men over the age of 60 years have an occult aortic aneurysm in the size range 4.0-5.9cm (Trial Participants 1998). AAA is 10 times more common in 65- to 75-year-old men compared to women of the same age (Crawford et al 2003). The gender-related difference in AAA incidence diminishes to about 3:1 in the 85 to 89-year-old age group (Collin et al 1988).

1.3 Death from Abdominal Aortic Aneurysm

AAA (with elective repair or rupture) is the 10th to 13th leading cause of death in the United States (Reilly et al 1989). The death rate for AAA (rupture) in the United Kingdom peaks at 65 to 75 years of age; rupture accounts for 1.7% of all deaths in men in this age group in the United Kingdom. Death from AAA in England and Wales showed a progressive and continuing increase over a 30-year period to 1988 (Collin 1988; Fowkes 1989). Age standardised death rates from ruptured AAA also rose by 2·4 per cent per year (Wilmink et al 1998), 20-fold in men and 11-fold in women between 1950 and 1984 (Fowkes et al 1989). Similar trends have been reported in other Western countries. The scale of the increase suggests that it is probably not simply an artefact of improved diagnosis (Coggon et al 1996). Moreover, a review of all post mortem examinations at Malmo General Hospital in Sweden during 1958-86 showed a clear rise in the prevalence

of aortic aneurysmal disease when assessed by standard examination techniques (Bengtsson et al 1992).

Rupture of AAA often has fatal consequences. Sudden loss of a large amount of blood results in haemorrhagic shock, with irreversible damage of vital organs, and cardiac arrest. Overall, an estimated 90% death rate if the rupture happened in the community or 50-60% death rate if the rupture occurred in a hospital having an emergency vascular service. Ruptured abdominal aortic aneurysms are estimated to contribute 1-2% of all male deaths over 65 years in Western countries (Goldstone et al 1993; Greenhalgh et al 1990). In the United States and the United Kingdom, approximately 15,000 and 10,000 people, respectively, die from ruptured abdominal aortic aneurysms each year (Goldstone et al 1993; Greenhalgh et al 1990). The overall mortality of ruptured abdominal aortic aneurysms varies between 85% and 95% (Johansson et al 1986; Budd et al 1989). The majority of patients die without ever reaching hospital and, of those who reach hospital alive, between 30% and 70% survive. A further reduction of the mortality has not been achieved in vascular surgery centres despite increasing experience, standardisation of the surgical technique and major advances in anaesthesia and intensive care medicine (Kniemeyer et al 2000).

1.4 Classification, Pathogenesis and Risk Factors for Abdominal Aortic Aneurysm

1.4.1 Classification

An aneurysm can be classified according to its site, morphology, and aetiology. 75% of abdominal aortic aneurysms are located below the renal arteries in the distal abdominal aorta (Dzau et al 1991).

According to its morphology, AAA can be classified as fusiform or saccular. Fusiform is the most common morphology of aneurysm. It is described as ovoid swelling affecting the entire circumference of a segment of arterial wall. Saccular is the less common form. It is an eccentric, localised, distended sac affecting only part of the circumference of the arterial wall (Zarins et al 2004).

A dissecting aneurysm usually occurs in the thoracic aorta. With the aortic dilatation, it has an intimal tear and separation of the layers of aortic wall, as a result, a false lumen within the aortic wall is created and compressed on the true lumen (Zarins et al 2004) (Figure 1.3).

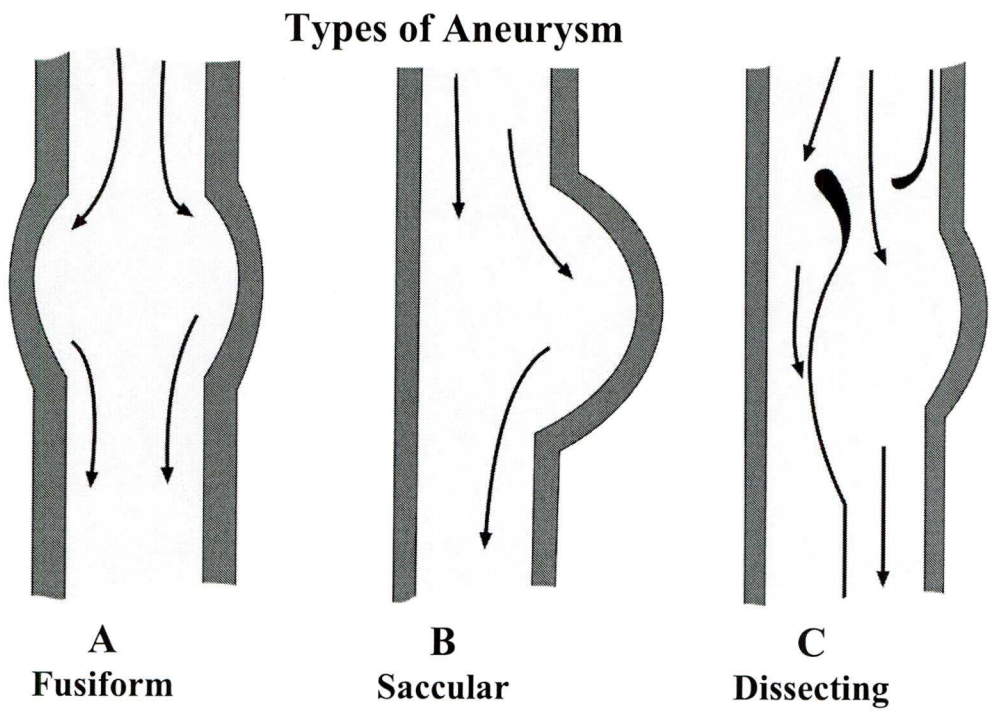

Figure 1.3: Diagram to show the different types of aortic aneurysm. (kindly provided by the department of medical illustration, Aberdeen Royal Infirmary).

Traditionally, AAA's have been associated with atherosclerotic disease and frequently referred to as atherosclerotic aneurysms. However, the atherosclerotic changes may be secondary to abdominal aortic aneurysms rather than being primary (Reilly et al 1989). Epidemiological characteristics and genetic risk factors are different in patients with AAA compared to those with stenosing arterial disease (MacSweeney et al 1994). The nutritional supply of the lower abdominal aorta depends on diffusion of nutrients from the aortic lumen, because the vasa vasorum (a network of small blood vessels that supply large blood vessels) is deficient in this part of the aorta (Appleberg 1994). Impaired diffusion through damaged intima, atherosclerotic plaques and overlying thrombi, and vessel wall vibration may further weaken the aortic media and facilitate the development of infrarenal abdominal aortic aneurysm (Appleberg et al 1994; MacSweeney et al 1994).

An inflammatory aneurysm is defined by presence of a thickened aneurysm wall, marked peri-aneurysmal and retroperitoneal fibrosis and dense adhesions to adjacent abdominal organs (Sterpetti et al 1989). Although this inflammation is more pronounced in 'Inflammatory AAA's' current understanding favours one pathological process with varying degrees of inflammation, rather than the distinct clinical entity (Rose et al1981). Contemporary study has corroborated this theory by demonstrating identical HLA alleles functioning in both inflammatory and degenerative AAA's, supporting the concept of a common immune-mediated pathogenesis (Rasmussen 2001).

Aneurysm can also occur in patients with Ehlers-Danlos and Marfan's syndrome. Marfan's syndrome results from a mutation in the gene codes for fibrillin, a family of connective tissue proteins that serve as scaffolding for the deposition of elastin during embryonic development. This genetic mutation weakens the aortic media and dilatation occurs, resulting in a high incidence of dissecting aneurysms, especially in the ascending aorta. The Ehlers-Danlos are a rare group of disorders characterized by hyperelasticity and fragility of the skin, joint hypermobility, and a bleeding diathesis. Ehlers-Danlos IV is associated with a tendency to spontaneous rupture of large arteries (Farber et al 1995).

Mycotic aneurysm is referred to as segment arterial wall dilatation as the result of localised sepsis. Most patients are elderly men with multiple comorbidities at presentation, most notably diabetes and hypertension, it can also occur in intravenous drug users (Luis et al 2010).

1.4.2 Pathogenesis

The pathogenesis of AAA is a multifactorial process. It involves genetic factors, ageing, atherosclerosis, inflammation, and localised proteolytic enzyme activation (Zarins et al 2004).

Elastin and collagen are important structural components of the aortic wall. Elastin is easily stretched and provides the elastic recoil of large arteries, while aortic collagen is coiled such that the initial load in the aorta is borne by elastin. As the vessel continues to stretch, collagen fibres become load bearing. Aortic collagen has a tensile strength over 20 times greater than that of elastin, but cannot extend beyond a small proportion of its original length before structural damage occurs. Initially, destruction of elastin shifts the load of pulsatile blood flow in the lower aorta from elastin to collagen. Part of the marked stiffness or inelasticity of dilated or aneurysmal vessels is attributable to this loss of elastin. Years of pulsatile blood flow through the degenerated vessel wall exacerbate the process, and the collagen is continuously exposed to the expansile force of intraluminal blood pressure.

Familial clustering of AAA suggests a genetic basis to this disease. Inherited defects in elastin and collagen might weaken the aortic wall, or genetic variables may increase enzymatic destruction of vessel wall constituents (Kent et al, 2010).

Both X-linked and autosomal dominant modes of inheritance have been suggested (Tilson et al 1984).

1.4.3 Risk factors

Documented risk factors for AAA are age, male sex, family history, previous vascular disease, smoking, hypercholesterolaemia and excessive weight (Kent et al, 2010; Lindholt et al 1996; R Darling et al; Adams et al 1993; Fitzgerald et al 1995).

Advancing age is an important risk factor for the development of an AAA (Wilmink, 1998). In population screening surveys, an AAA is six times commoner in men than women (Pleumeekers et al, 1995; Scott et al, 1995), but it is only twice as common in men in post mortem studies (McFarlane 1991; Bengtsson 1992). In England and Wales, the age-standardized mortality rate of AAA is twice as high in men as women (Statistics 1995). AAA is uncommon before 50 years of age. Normal ageing is associated with alterations in the structure and, consequently, the mechanical properties of the aortic wall. Thus, the ageing aorta may be less able to withstand the force of pulsatile blood flow, resulting in aneurysmal dilatation (MacSweeney et al 1994).

Cigarette smoking has been strongly associated with the presence of AAA, aneurysm expansion rates, and death from aneurysm rupture. The mechanism is thought to be enhancement of proteolytic enzyme degradation of the aortic wall by gaseous and blood-borne products of tobacco combustion (Collin et al, 1988;

MacSweeney et al, 1994). The only prophylactic advice that appears useful is cessation of smoking (Cheatle et al 1989).

Hypertension is associated with increased prevalence and increased risk of rupture. Hypertension may be related directly to pathogenesis or may merely exacerbate the effect of blood flow forces on an already weakened aortic wall (MacSweeney et al 1994).

1.5 Clinical Presentation and Examination

Most unruptured AAA's are asymptomatic. Approximately 75% of abdominal aortic aneurysms are asymptomatic at initial diagnosis (Thompson et al 2001). A feeling of fullness or pulsations in the abdomen may be early symptoms (Zipes et al 1990). Inflammatory aneurysm may present with history of vague abdominal or back pain, general malaise and weight loss, sometimes it can present as ureteric obstruction as the primary complaint. Rapid expansion of an abdominal aneurysm may cause intense pain that is exacerbated by pressure over the aorta (Thompson et al 2001).

Typically, ruptured abdominal aortic aneurysm presents with sudden onset, acute epigastric pain, with or without back pain. Often the patient will have a history of collapse, but haemodynamic disturbance may not present at all in some cases. The clinician should consider the possibility of rupture of an AAA in any male

patient over the age of 60 years who presents with sudden onset epigastric and/or back pain with or without shock and/or collapse (Duthie et al 1988; Appleberg et al 1994). In addition, patient characteristics which may raise clinical suspicion of AAA include being a current smoker or with a significant smoking history, a history of myocardial infarction (Lederle et al 1988) and claudication (Simon et al 1996). As discussed above, a strong familial occurrence of AAA should also raise diagnostic suspicion, as should the presence of hypertension (Reilly et al 1989).

Physical examination of AAA has low overall sensitivity. A study to determine the accuracy of physical examination in AAA detection found that abdominal palpation detected only half of 18 previously unsuspected aneurysms in 201 patients. This study found that abdominal girth was an important factor in detecting AAA by physical examination (Lederle et al 1988).

1.6 Unusual Clinical Presentations

Unusual clinical presentations of AAA may result from chronic contained rupture, aortoenteral fistula, and thrombo-embolism. These manifestations may complicate surgery and raise operative morbidity and mortality. A chronic contained rupture may, in addition to abdominal or low back pain, cause pressure effects resulting in jaundice from common bile duct compression or ureteric obstruction, femoral neuropathy, or extension of the haematoma into the femoral sheath, simulating a groin hernia. (Bower et al, 1989).

Aortocaval and aortorenal vein fistulas result from rupture of an AAA into the inferior vena cava or the left renal vein. Clinical presentation includes high-output heart failure, cardiomegaly, a palpable abdominal mass, audible continuous bruit, hypotension, oliguria, and abdominal and back pain(Bower et al. 1989).

Mycotic aneurysms are rare and may result from superimposed infection or arise secondarily from an infection. Clinically, infected aneurysms may present with the sudden appearance of a pulsatile mass or recent enlargement of a known AAA in combination with fever or recent febrile illness (Bower et al. 1989).

Thrombo-embolism from an abdominal aortic aneurysm to one or both of the lower extremities is a well recognised phenomenon, (Bower et al 1989). Thrombus within the lumen of the aneurysm or cholesterol debris from within the intima of the wall can be the source of macroemboli or microemboli, respectively. Macroembolism presents with symptoms and signs of large-vessel occlusion and sudden ischemia of the lower limbs. Small-vessel occlusion resulting from microemboli presents as slowly evolving livedo reticularis, painful cyanotic toes, and palpable pedal pulses. Microembolism has been termed blue toe syndrome because of the characteristic cyanosis of the toes; if both lower extremities are involved, an aortic or cardiac source should be considered (Bower et al 1989).

Other unusual complications of AAA's include recurrent ischaemic myelopathy and/or paraparesis. Ischemic spinal cord lesions may present with bladder

incontinence and patchy sensory loss (Desai et al 1989). Paraparesis may result from anterior spinal artery syndrome, which presents as a varying degree of muscle weakness and associated sensory loss of pain with sparing of proprioception (Joseph et al 1989).

1.7 Imaging for Abdominal Aortic Aneurysm

There are many methods available for imaging the aorta; each with strengths and weaknesses. The choice is dependent on individual cases, equipment availability, technical expertise, and surgeon preference; all should influence imaging modality selection (LaRoy, Cormier et al. 1989).

1.7.1 Plain abdominal X ray

Abdominal aortic aneurysms can be noted on antero-posterior (Amparo et al, 1985) plain x-ray. Most AAA's occur between the renal arteries and the iliac bifurcation; that is, between the L2 and L4 vertebral levels, respectively. In the frontal (AP) projection, an AAA is usually seen on the left side of the spine and appears as a soft tissue density demarcated by a thin, curvilinear rim of continuous or discontinuous calcification (figure 1.4). Calcification is noted in 55% to 85% of AAA's (Brewster 1976; LaRoy, Cormier et al. 1989); in the remainder, a soft tissue density may be identifiable. Erosion of the anterior margins of the vertebral bodies may be noted with inflammatory and saccular aneurysms, and those involving contained rupture (Nonami et al, 1996; Yochum et al 1996).

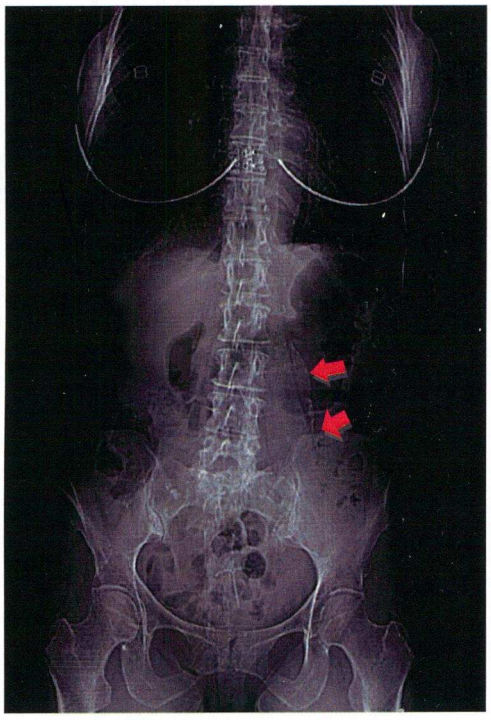

Fig1.4. Antero-posterior plain abdominal pelvis X-ray showing: Curvilinear rim of discontinuous calcification in the wall of an AAA (two red arrows); maximum transverse diameter 7.5 cm.

1.7.2 Ultrasound / Duplex

Ultrasound scanning is currently the most practical and accurate way of detecting abdominal aortic aneurysms in large numbers of people (Graham and Chan 1988), and has become the most commonly used method of screening (Graham and Chan 1988; LaRoy, Cormier et al. 1989; Wong 2000). Ultrasound enables diagnostic confirmation, evaluation of size, and monitoring of progression (Graham and Chan 1988). However, the accuracy of ultrasound is operator-dependent and the results may vary between vascular centres or even within centres, especially when the aneurysm is small (Ellis et al 1991: Andrew et al 1995).

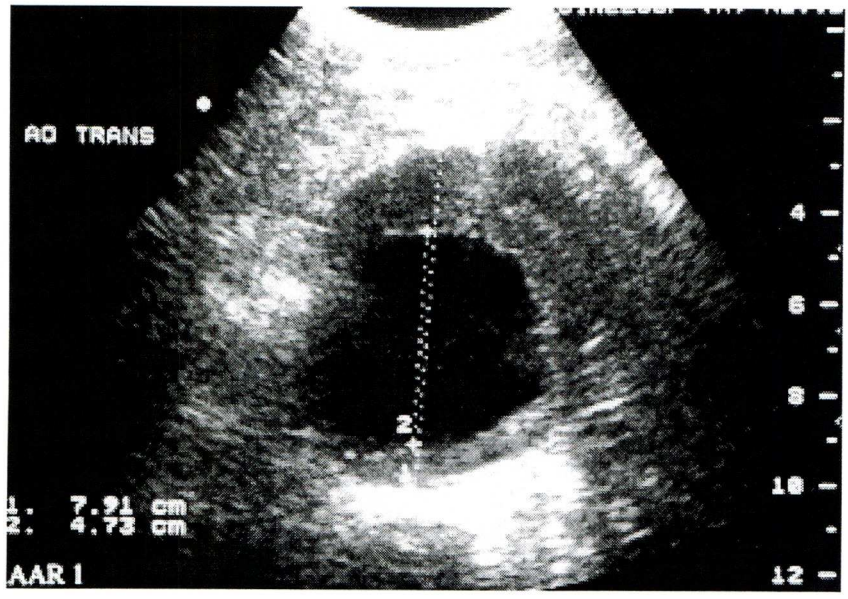

Figure 1.5: Ultrasound of a large AAA. The Anteroposterior diameter of this AAA measures 7.91 cm; intraluminal diameter is 4.73 cm. Intraluminal thrombus is clearly visible.

1.7.3 Computed tomography (CT)

With the improvement of technology, especially the availability of new high speed spiral CT, CT has become the "gold standard" in the preoperative assessment and postoperative evaluation of AAA's. Enhanced with contrast, CT can accurately demonstrate the size and craniocaudal extent of an abdominal aortic aneurysm and is able to detect intraluminal thrombus. Aortic aneurysm neck, iliac artery dimensions, angulation and presence of thromboses can also be demonstrated accurately. Furthermore, contrast enhanced spiral CT (CTA) scanning can also produce a computerized 3D model which can provide the level of accuracy needed for successful endovascular treatment of AAA's (Beebe et al, 2000).

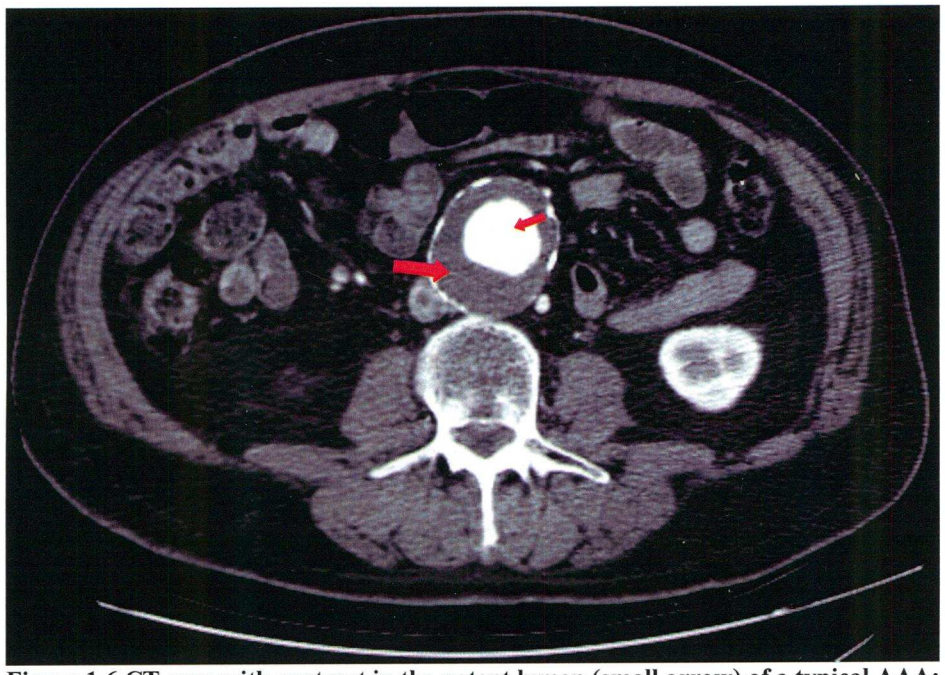

Figure 1.6 CT scan with contrast in the patent lumen (small arrow) of a typical AAA; thrombus (large arrow).

1.7.4 Magnetic resonance imaging (MRI)

The multiplanar display capability of magnetic resonance imaging (MRI) can demonstrate the aorta and surrounding soft tissue anatomy accurately without the need for contrast. It allows accurate measurement, isolates flow abnormalities, identifies clot, and allows assessment of visceral involvement (Yochum 1996).

Gadolinium-enhanced magnetic resonance angiography (MRA) is a variation of standard MRI, utilizing a paramagnetic contrast agent. This modality provides anatomic information for aortic reconstructive surgery without the contrast-related renal toxicity or catheterization-related complications as seen in CTA and conventional angiography, (Prince, Narasimham et al. 1995).

As with contrast enhanced spiral CT (CTA), MRA has become the "gold standard" for the preoperative assessment and postoperative evaluation of AAA's in some centres. The choice between CTA and MRA is largely dependent on local experience and the availability of the latest scanner. At present there is no consensus to indicate the superiority of either modality (Hirsch et al, 2006)

1.7.5 Aortic digital subtraction angiography

Aortoangiography is used to evaluate the state of the renal arteries and other vessels in the iliac artery system in patients with AAA (Appleberg 1994). (Figure 1.7) However, its role in the preoperative assessment and postoperative evaluation of AAA has largely been replaced by CTA and MRA.

However, aortoangiography may underdemonstrate the size and extent of the thrombus-filled aneurysm, as only the lumen is demonstrated (LaRoy, Cormier et al. 1989). Currently, aortoangiography is only sometimes used for anatomical measurements in planning for endovascular repair of abdominal aortic aneurysm.

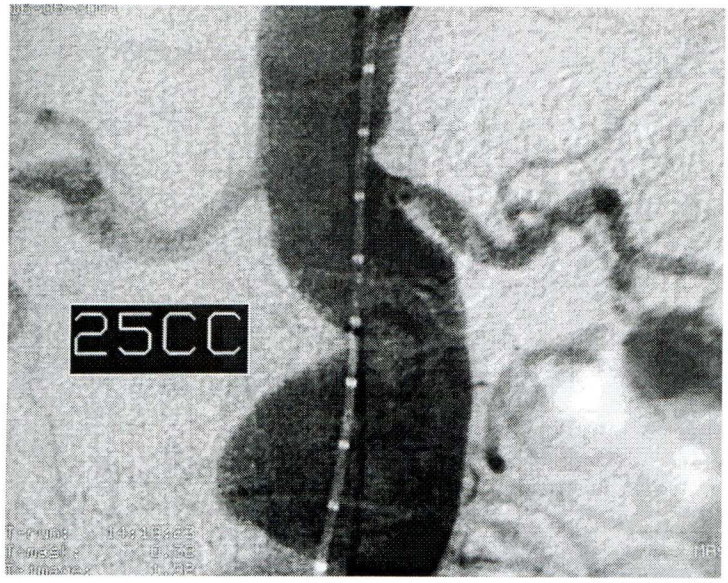

Figure 1.7 Angiogram showing a large abdominal aortic aneurysm.

1.8 Natural History of Abdominal Aortic Aneurysm

Most AAA's continue to enlarge progressively. Small aneurysms increase in transverse diameter by 2-3 mm on average, per year (Cronenwett et al 1985; Cook et al 1996); whilst the anteroposterior diameter increases by an average of 2.2 mm, per year (Cronenwett et al 1985). Large aneurysms expand more rapidly than smaller ones (Appleberg et al 1994; Cook et al 1996).

The estimated aneurysm expansion rate based on its diameter is given in Table 1.1

Size	Annual expansion rate
Less than 4 cm	0.2 - 0.4cm
4-5 cm	0.2 - 0.5cm
More than 5cm	0.3 - 0.7cm

Table 1.1 Aneurysm annual expansion rate based on its diameter (Hallin 2001)

The most established method to assess probability of rupture of AAA is the diameter of the aneurysm, but it is still unclear whether the rate of aneurysm rupture correlates with the aneurysm size. In particular, in aneurysms larger than 5.0cm diameter a study has suggested that rupture rate is typically 25–40% at 5 years, but only 5–7% for aneurysms of 3.5–5.0cm, and approaching 0% for aneurysms less than 3.5cm (Wyffels et al 2000).

Life expectancy of aortic aneurysm patients is shorter than in those of similar age and sex who do not have an aortic aneurysm, due to their life threatening co-morbidities (Koskas et al 1997). Deaths from the other cardiovascular conditions are the major reason for the reduction of life expectancy (Brady et al 2001).

1.9 Principle of Management of Abdominal Aortic Aneurysm

Since ruptured abdominal aortic aneurysms cause significant mortality, especially outside the hospital environment, the principal aim of managing AAA's must therefore be to decrease the rate of aneurysmal rupture.

Evidence of risk of rupture of small AAA's (4.0 to 5.4cm) has been provided by a small aneurysm trial in the UK and ADAM (Aneurysm Detection and Management Study) from the USA (Trial Participants 1998; Lederle et al. 2002). The results and design of the two studies are very similar. Both trials concluded that surveillance of AAA's of 4.0 to 5.5cm was safe in compliant patients, and that early surgery did not result in any long-term survival advantage. An additional important observation from the UK small aneurysms trial was that death was attributable to ruptured AAA in 5% of men who died, but 14% of women who died (Trial Participants 1998). The risk of rupture was 4 times higher among women, than men. The trial participants concluded that the threshold of 5.5 cm diameter may be too high for women.

The following principles of management of AAA have been suggested to reduce the mortality from rupture (Thompson 2001).

1): Adoption of national screening programmes to identify patients with asymptomatic aneurysms in a community setting.

2): Medical treatment of small aneurysms detected in a screening programme to reduce expansion and rupture rates.

3): Selection of appropriate patients for surgery so that operative risk is balanced against the risk of rupture.

4): Reduction in the mortality rates of elective and emergency surgery for AAA's.

1.10 Conventional Surgical Management of Uncomplicated Abdominal Aortic Aneurysm

1.10.1 Historic review

Arterial aneurysms have been recognized since ancient times. One of the earliest texts known, the Ebers Papyrus (200 BC), contains a description of traumatic aneurysms of the peripheral arteries (Osler 1905). However, not until the 16th century, came the first description of abdominal aortic aneurysm, by anatomist Vesalius (Leonando 1943). The first elective operation for treatment of an aneurysm was reported by Antyllus in the 2nd century AD. He recommended ligating the artery above and below the aneurysm and then incising the sac and evacuating its contents (Osler 1915).

There were a few early attempts to repair the aneurysm. Cooper attempted to ligate the aneurysm in 1817. Matas performed endoaneurysmorrhaphy, which

consisted of imbrication of the opened aneurysm edges in1906. Rea, in1948, performed cellophane wrapping (Zarins et al 2004).

The 1st modern repair of an abdominal aortic aneurysm was performed on March 29th 1951, in Paris, by French physician Charles Dubost. His patient was a 50-year-old man, and the operation was performed via a left thoracoabdominal incision. A 15-cm homograft, taken from the thoracic aorta of a 20-year-old woman who died 3 weeks earlier, was anastomosed to the aorta and right common iliac artery. An endarterectomy of the occluded left common iliac artery was performed before its anastomosis to the homograft (Dubost, 1952). The patient survived for 8 years and died from a myocardial infarction at his home, in Brittany. The report of this operation rocked the surgical world and inspired surgeons throughout Europe and the United States. Several years later, Michael DeBakey performed a similar operation with a polyester fabric prosthesis and coined it "Dubost's operation" (Friedman, 2001). However, dissection and removal of the aneurysm still was a major operation with a large volume of blood loss. Greech introduced the 'inlay graft technique' which is a simplified version of "Dubost's operation" (Greech 1996). This technique was popularized by Orr and Davies (Orr et al. 1974). Initially, the mortality rate following open surgery was 20 percent, but gradually improved, so that surgical repair became standard treatment (Crawford et al. 1981)

1.10.2 Patient selection

The indication for surgical repair for asymptomatic AAA's is based on size ≥ 5.5cm. This was based on the results of UK small aneurysm trials and it was further confirmed by the ADAM trial from the United States and patients' general fitness. However, there is no universal standard for selection of patients for surgical intervention. The Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery has produced guidelines with recommendations for the treatment of abdominal aortic aneurysm (Hirsch et al, 2006).

1: The arbitrary setting of a single threshold diameter for elective AAA repair applicable to all patients is not appropriate, as the decision for repair must be individualized.

2: Randomized trials have shown that the risk of rupture of small (5 cm) AAA's is quite low, and that a policy of careful surveillance up to a diameter of 5.5 cm is safe, unless rapid expansion (1 cm/yr), or symptoms, develop. However, early surgery is comparable to surveillance with later surgery, so that patient preference is important, especially for AAA's 4.5 cm to 5.5 cm in diameter.

3: Based on the best available current evidence, 5.5cm diameter appears to be an appropriate threshold for repair in an "average" patient. However, subsets of younger low-risk patients, with long projected life expectancy, may prefer early repair. If the surgeon's personal documented operative mortality rate is low, repair may be indicated at smaller sizes (4.5-5.4 cm) if that is the patient's preference.

4: For women, or AAA with greater than average rupture risk, elective repair at 4.5 cm to 5.0 cm is an appropriate threshold for repair.

5: For high-risk patients, delay in repair until larger diameter is warranted.

1.10.3 Standard open surgical technique- 'Inlay Graft Repair'

Figure 1.9 briefly describes the techniques of abdominal aortic aneurysm repair. A large abdominal midline or transverse incision was made to access the abdominal cavity. This was then followed by mobilising the retroperitoneum and duodenum to expose the aortic aneurysm with normal aorta above and both iliac arteries below. After isolating the aneurysm by clamping the aorta just above the aneurysm and both iliac arteries, the aneurysm was then opened along its axial direction and its content was removed. Any back bleeding from branches which open into the aneurysm sac, such as lumbar arteries and inferior mesenteric artery, were sutured; some surgeons prefer to ligate the inferior mesenteric artery before opening the aneurysm sac. After a normal segment of aorta between the clamps was adequately exposed, a prosthetic tube graft was then sutured onto it by hand anastomosis and blood flow restored by releasing the clamps. Sometimes, when there were no normal segments in the distal end of aorta or even the iliac arteries available, it was necessary to use bifurcated prosthetic graft to suture the distal end onto the iliac arteries, or even more distally. After thorough checks for any bleeding with further necessary sutures, the aneurysm sac was then closed to cover the prosthetic graft and the suturing sites.

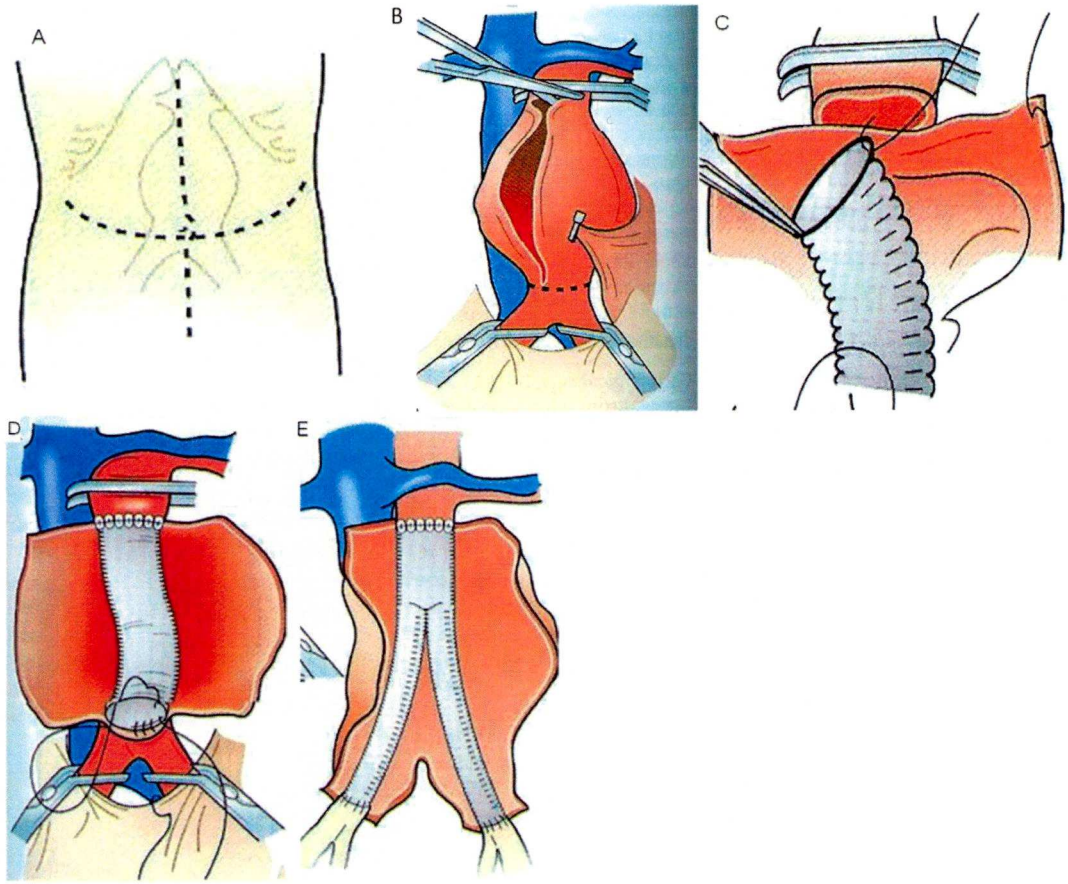

Figure 1.9: Operative technique of open abdominal aortic aneurysm repair, A, The Aneurysm is approached through a midline or transverse transabdominal incision or a left flank retroperitoneal incision. B: Proximal and distal control is obtained, the aneurysm is opened, mural thrombus is removed, and back bleeding lumbar orifices are oversewn, C: The proximal anastomosis is started along the back wall of the aorta as shown, or the proximal neck is transacted and end-to-end anastomosis is created. D, The distal anastomosis is constructed in a similar fashion; if backbleeding from the inferior mesenteric artery (IMA) is pulsatile and the hypogastric arteries are patent, the IMA may be oversewn. E. If the iliac arteries are aneurysmal, a bifurcated prosthetic graft is used. (Zarins et al 2004)

In repair of abdominal aortic aneurysm, the aneurysm can also be accessed by smaller incisions (mini laparotomy incision), retroperitoneal approach, laparoscopic or laparoscopic assisted approaches. However, all these different approaches have a similar way to repair the aneurysm, and they all have different advantages and disadvantages.

1.11 Outcomes of Open Repair of Abdominal Aortic Aneurysm

Open abdominal aortic aneurysm repair carries a considerably high risk of mortality and morbidity. To repair the abdominal aortic aneurysm, a large abdominal incision is required. This can cause significant pain and restrict respiratory movement. In addition, a high number of patients suffer undiagnosed COPD (Chronic Obstructive Pulmonary Disease), so, respiratory complications after open abdominal aortic aneurysm repair are common. Clamping and de-clamping the aorta has a significant impact on the heart, due to the sudden change in circulating volume which, may cause cardiac complications. Furthermore, open abdominal aortic surgery can cause systemic inflammatory response syndrome which is the reason for developing multiple organ failure (MOF). MOF is one of the leading causes of death after open abdominal aortic aneurysm repair.

1.11.1 Perioperative mortality

The operative mortality rate after open AAA repair has changed little over the last two decades, despite the advances in perioperative care (Bradbury et al 1998). The reported mortality rate varies among hospitals and groups.

In the United Kingdom there are two multicentre, randomized, controlled trials compare the outcomes of endovascular or open repair of abdominal aortic aneurysms (details will be discussed in chapter 2). The reported 30-day mortality from one trial is 4.7% in the open-repair group (Greenhalgh et al, 2004). Another

study reviewed 37,654 patients in seventy-two papers. The authors analysed the results according to the type of study designs. They found that there is clear and consistent disagreement in reported mortality rates between hospital-based and population-based studies of elective surgery for AAA. The mortality in the population-based study was 7.0%-10.6% with a mean of 8.2%, while hospital-based mortality was 3.0% - 4.8% with a mean of 3.6% (Blankensteijn et al 1998). Furthermore, since the hospitals and groups with high mortality are unlikely to publish their results, the actual mortality rate is likely to be higher in everyday vascular surgical practice than those reported in medical journals.

1.11.2 Perioperative morbidity

The overall morbidity rate after elective aneurysm repair is 10% to 30%. The most frequent complication is myocardial ischaemia, which usually occurs within the first 2-4 days after surgery. Myocardial infarction is also the most common cause of postoperative death (Zarins et al 2004). Irregular heart rhythm and heart failure are also commonly occurring cardiac complications. Mild renal failure is the second most frequent complication. It is more frequent with pre-existing renal disease and may occur as a result of hypoperfusion, systemic inflammatory response syndrome and occasionally, atheroembolism. However, severe renal failure, requiring long term dialysis, is rare. The third most common group of complications is respiratory. Post operative acute lung injury from the systemic inflammatory response syndrome is one of the most commonly occurring respiratory complications. Acute lung injury may lead to "Acute respiratory distress syndrome" and being prone to infection. Post operative pneumonia and acute pulmonary embolism following a deep vein thrombosis are also frequent

occurrences. However, with proper patient selection and care, respiratory failure as the principal cause of death is rare (Zarins C K et al 2004).

Other complications including bleeding (from aneurysm repair site or gastro-intestinal tract), cerebrovascular accident, prolonged bowel dysfunction, and bowel ischaemia may also occur postoperatively. Sexual dysfunction is also frequently-occurring after open repair of AAA. Symptoms mainly present as impotence, which may be psychological, neurological, or relating to reduced internal iliac artery perfusion; or as retrograde ejaculation, which is related to nerve injury in the vicinity of the left common iliac artery.

Local complications after open repair of AAA include limb ischaemia, bleeding from anastomosis, wound infection, graft infection, thrombosis and wound dehiscence. A study reviewed 37,654 patients in seventy-two papers concerning results of open AAA repair over an eleven year period. The systemic and local complication rates are given in Table 1.2 (Blankensteijn 1998).

System complications	Frequency (%) medial (Range)
Cardiac	12.0 (10.5-13.9)
Pulmonary	9.8 (8.3-11.6)
Renal	4.8 (3.8-6.2)
Gastrointestinal	13.0 (11.3-14.9)
Cerebral	0.6 (0.3-1.5)
Local vascular complications	
Limb ischaemia	5.8 (4.2-7.9)
Bleeding	6.2 4.7-8.1)
Wound infection	1.5 (0.9-2.5)
Graft infection	0.3 (0.1-1.0)
Thrombosis	1.1 (0.6-2.0)
Wound dehiscence	0.6 (0.3-1.3)

Table 1.2 Reported complications following elective open repair of AAA.

1.11.3 Long-term results of open repair

In general, the long term outcome of open abdominal aortic aneurysm repair is good. A population based study followed 208 patients after open repair of their abdominal aortic aneurysm. Patients were followed for 15 years. The 5-year, 10-year and 15-year survival, free from any vascular reintervention rates were 91.5%, 86.2% and 72.0% (Biancari et al 2002). Authors concluded that open repair of Infrarenal AAA's can achieve satisfactory 15-year follow-up rates of survival, free from reintervention for any graft-related complications. A study from Crawford et al has also produced similar results, (Crawford 1981).

Long term complications include aorto-enteric fistula, graft infection, false aneurysm formation and aneurysm rupture. These complications are generally rare, though can be fatal when occurring.

1.12 Summary

Aortic aneurysm is a common disorder among the elderly population. The incidence of aortic aneurysm has increased rapidly over recent years. Most aortic aneurysms do not present any symptoms, until rupture. If untreated, aortic aneurysms will continuously grow and most of them will eventually rupture. Open surgical repair has become a well established technique for over fifty years. It is effective to prevent aneurysm rupture, but it is a complicated major operation, carrying significant morbidity and mortality. The outcome of open repair of aortic aneurysm has changed little over the last two decades.

CHAPTER 2

ENDOVASCULAR ABDOMINAL AORTIC ANEURYSM REPAIR (EVAR)

2.1. Development of Endovascular Abdominal Aortic Aneurysm Repair

2.1.1 Historical Review

As mentioned in the previous chapter, the natural history of an abdominal aortic aneurysm (AAA) is progressive enlargement, until it ruptures. The mortality is around 50% in patients who have a contained rupture and make it to hospital (Johansen, et al, 1991; Kniemeyer, et al, 2000; Noel, et al 2000; Heller,et al, 2001), the overall mortality may be as high as 90% (Johansen, et al, 1991; Kniemeyer, et al, 2000; Noel, et al, 2000). Therefore, the primary objective in the management of a diagnosed AAA, is to prevent death from rupture. Deaths from ruptured AAA are the third commonest cause of non-accidental sudden death in the United Kingdom, after coronary artery disease and stroke (Noel, et al 2000).

The management options for an unruptured abdominal aortic aneurysm previously consisted of open repair or "best medical treatment" which included regular ultrasound scan surveillance and risk factor modifications. Standard surgical repair, involving a large abdominal incision and cross-clamping of the aorta, is frequently complicated and has an average in-hospital mortality of approximately 2% to 6% (Hollier, et al 1986). With an ageing population, the number of high risk cases also increases thereby resulting in higher mortality. Average blood loss is

2–3 units in 95% of cases, with an average hospital stay of 6 days (Wyffels P, et al; 2000; Hollier, et al 1986). Laparoscopic aortic aneurysm repair has been developed recently, and a lower perioperative mortality has been reported (Cau, et al, 2006). However, due to the complexity of the technique and the lengthy operation, this technique has not gained popularity.

Since endovascular aortic aneurysm repair (EVAR) has been developed, it has provided vascular surgeons with an alternative method to conventional open surgery in treating aortic aneurysm disease.

Endovascular approach to arteries is a long established technique in clinical practice; with introduction of guide-wires and catheters. By injecting radio-opaque contrast media, the relevant arteries can be imaged and subsequent therapeutic procedures performed. With the introduction of digital subtraction angiography, (DSA), (a method in X-Ray imaging, which allows irrelevant parts of the anatomy to be "subtracted", so the relevant parts can be shown much more clearly), the quality of vascular imaging using X-rays has become better than ever before.

With this technology, Parodi, and independently Volodos, proposed a new method of treating AAA. Their concept was to combine endovascular and minimally invasive techniques (Parodi, et al, 1991; Volodos, et al, 1991). This new technique involved the transfemoral or transiliac placement of a stent-graft within the aneurysm, via two small incisions made in the patient's groin. The aim of the treatment is to achieve complete exclusion of the aneurysm sac from the circulation, thereby protecting the aneurysm from rupture. At the same time the aneurysm sac and its contents remain in situ. The stent-graft is usually

compressed into a plastic sheath, inside which it is delivered into the aneurysm and manoeuvred into position under X-ray (fluoroscopy) guidance. It is then deployed by withdrawal of the sheath, and other triggering devices. After final fixation at the proximal and distal ends of the stent-graft, it is sometimes necessary to inflate a moulding balloon inside the stent-graft at the attachment zone to ensure a secure seal. Some devices also have additional fixation appendages to anchor the stent-graft to the aortic wall. This operation can be performed under general, regional or local anaesthesia. Nowadays, some devices can even been inserted percutaneously without an incision in the groin.

The stent-graft is a prosthetic vascular graft, (typically made of Dacron or polytetrafluoroethylene), which is reinforced by metallic struts. In general, endovascular stent-grafts fall into three broad categories: (i) bifurcated or tubular unibody grafts. (ii) Modular multicomponent grafts. (iii) aorto unilateral grafts with a contralateral iliac occlude, which are followed by surgical femoro-femoral bypass (Veith, et al, 1999).

2.1.2 Development of stent-graft for endovascular abdominal aortic aneurysm repair

Following the publication from Parodi and Volodos of results using their "home made" device, the endovascular stent-graft became rapidly commercialised. The first tube graft development by Endovascular Technologies (later to be taken over by Guidant, Menlo Park, CA, USA) was implanted in 1993. This graft was then further developed into the Ancure device, which has now been withdrawn from the market due to a high incidence of device malfunction and other adverse events, and failing to report to the FDA. Since 1993, around 15 other types of stent-grafts have been developed and come to the market. All these stent-grafts claim an

advantage over the others (Rutherford et al, 2004). Some, however, have followed the Ancure stent-graft and have been withdrawn from the market. These include the Vanguard (Boston Scientific, Natick, MA, USA), all of which had design flaws, and caused an increased risk to the patient as compared with open repair. In addition, high development costs have seen the withdrawal of the Lifepath by Edwards Lifescience (part of Baxter Healthcare Corp. Irvine, CA, USA), even though the Lifepath later had positive results from its clinical trial (Carpenter et al, 2004).

2.2. Principle of Endovascular Repair of Abdominal Aortic Aneurysm

2.2.1. Aim of endovascular repair of abdominal aortic aneurysm

As mentioned before, the aim of EVAR is to prevent the aneurysm from rupturing by completely and permanently excluding it from the pressure and flow of the blood circulation, without causing disruption to any important visceral blood supply. To achieve this, it is essential to meet the following criteria:

(i) Seal: The aneurysm sac must be completely sealed from the blood pressure and flow.

(ii) Fixation: The seal must be maintained by a good fixation against the downstream blood flow throughout the patient's life.

(iii) Maintenance: All important visceral blood supply must be maintained.

2.2.2. Patient selection

Currently, there are no generally agreed indications for EVAR between different units and countries. But, as for open repair, patients with infrarenal abdominal aortic aneurysms more than 5.5cm in diameter are considered for EVAR in most centres.

Due to the minimally invasive nature, patients selected for EVAR have fewer requirements on cardiovascular function, pulmonary function and general fitness. However, there are no commonly agreed selection criteria for patients receiving EVAR. The best evidence available is from the UK EVAR-2 trial which suggested that patients who are not fit for open repair will not benefit from EVAR since most patients will die from causes other than their aneurysm (EVAR trial participants, 2005). But due to controversies surrounding the trial design and data interpretation, many vascular centres do not follow this recommendation.

2.2.3. Anatomical consideration

Anatomical suitability for EVAR is based principally on the morphology of the aneurysm, the length and character of proximal (aortic neck) and distal landing zones, such as degree of angulation, calcification, thrombosis and conical shape of aortic neck and the tortuosity of iliac arteries. The diameter, length, angulation, presence of calcification and mural thrombus in the aortic neck are the most frequent cause of exclusion from EVAR (Arko et al, 2004; Lezzi R et al, 2006). A study suggests that 55% patients were considered suitable for EVAR and 45% patients deemed ineligible (Arko et al 2004). The most common anatomical reason for ineligibility was a short infrarenal neck (44%), a large proximal neck diameter (25%), iliac aneurysms (10%), extremely tortuous or calcified neck (7%), iliac occlusion (6%), and small distal aortic bifurcation and accessory renal arteries (5%). Similarly, Carpenter et al (Carpenter et al, 2001) reported short aneurysm neck (54%), inadequate access from small iliac arteries (47%), wide aneurysm neck (40%), bilateral common iliac artery aneurysms (21%), excessive neck angulation (14%), excessive mural thrombus in aneurysm neck (10%), and accessory renal arteries (6%) with many patients having a combination of factors.

With increasing clinical experience, and improvement in stent-graft design that is constantly providing new and versatile devices, the number of patients eligible for

EVAR has increased and more and more anatomical limitations have been overcome. However, complex aortic anatomy will still be a significant limitation for the foreseeable future.

2.3. Currently Commonly Used Stent-grafts and their Configurations

The following lists the currently commonly used stent-graft devices in the UK, and their configurations (Table 2.1)

Company	Device	Fixation location	Graft materials	Stent materials	Stent Expansion
Medtronic	AneuRx	Infrarenal	Woven polyester	Nitinol	Self-Expanding
Lombard medical	Aorfix	Infrarenal	Woven polyester	Nitinol	Self-Expanding
Gore	Excluder	Infrarenal	ePTFE	Nitinol	Self-Expanding
Medtronic	Endurant	Suprarenal	Woven polyester	Nitinol	Self-Expanding/ Suprarenal barbs
Endologix	Powerlink	Infrarenal or Suprarenal	ePTFE	Stainless steel alloy	Self-Expanding
Medtronic	Talent	Suprarenal	Woven polyester	Nitinol	Self-Expanding
Cook	Zenith	Suprarenal	Woven polyester	Stainless Steel	Self-Expanding/ Suprarenal barbs

Table 2.1: Currently Commonly Used Stent-grafts in the UK, and their Configurations.

2.4. Early and Mid-term Results of EVAR

Since EVAR was first described in 1991, there have been many clinical papers dedicated to EVAR. Most of the studies have largely consisted of small case series investigating specific aspects of EVAR (usually in direct comparison with

conventional AAA repair). The smaller studies have provided some convincing evidence that the minimally invasive nature of EVAR, with no cross clamping at the aortic neck, in conjunction with obviation of the need for laparotomy and complex abdominal dissection, results in less physiological insult than open AAA repair. Biological markers of inflammatory pathways and stress responses such as proinflammatory cytokines, adrenaline, cortisol, and complement activity are reduced (Thompson, et al, 1999; Boyle, et al, 2000; Thompson et al, 1996). There is convincing evidence that EVAR is associated with reduced cardiac, respiratory, and renal complications, reduced need for blood transfusion and analgesia, shorter postoperative hospital stay, lower need for intensive care, a faster return to normal function, and lower infection rates (Prinssen, et al, 2004; Faries, et al, 2002; Boyle et al, 1997; Zarins, et al, 1999; Zeebregts et al, 2004; Elkouri et al, 2004).

Until the last few years, in the absence of evidence from large national randomised controlled trials, evidence on the efficacy and durability of EVAR relied upon individual institutional experience and data from large voluntary registries, such as the UK Registry for Endovascular Treatment of Aneurysms (RETA), and in particular, the European Collaborators on Stent Graft Techniques for Abdominal Aortic Aneurysm Repair (EUROSTAR) Registry (Carpenter et al, 2002; Thomas et al, 1999). EUROSTAR is a voluntary registry that has been prospectively collecting data on EVAR procedures performed in Europe since 1999, and has provided much of the current EVAR outcome data (Thomas et al, 1999: Harris et al, 1997). These sources have suggested that the initial operative mortality of EVAR was comparable to that of open AAA repair, but has consistently fallen, and may now be as low as 1% (Holzenbein et al, 2001; Harris et al, 2000; Zarins et al,

2002; Fammatter et al, 2002; Blum et al, 1997). However, it has been difficult to make early meaningful interpretation and comparison of the data from these registries and case series, because of factors such as publication bias, lack of patient randomisation, the likelihood of a large number of patients having small aneurysms, the inclusion of patients considered unfit for open AAA repair, and patients with less challenging anatomy (Carpenter, et al, 2000; Collin et al, 2001; Buth, et al, 2001).

In the United Kingdom there have been two multicentre, randomized, controlled trials; EVAR 1 and EVAR 2, both of which started in 1999. The trials, commissioned by the UK National Health Service's Health Technology Assessment Program at a cost of £1.7 million, were the largest of their kind in the world. EVAR 1 was the first trial to compare the two techniques and has been successful in recruiting a large number of patients and doctors.

EVAR 1 randomised patients with an AAA >5.5 cm, who were medically fit, and anatomically suitable for both open AAA repair (OR) and EVAR, to undergo one or other procedure. EVAR 2 randomised patients who were considered medically unfit for open AAA repair (but anatomically suitable for EVAR), to undergo EVAR or receive no intervention, between September 1999 and December 2003. EVAR 1 recruited 1082 patients (543 EVAR v 539 OR), EVAR 2 recruited 338 patients (166 EVAR v 172 no intervention), 60 years or older, from 41 centres. Also in Europe, the smaller Dutch DREAM trial randomised 345 patients to either open AAA repair or EVAR.

The short term (30 day mortality) outcome of these trials was published in 2004, with the EVAR 1 trial reporting a significantly improved 30 day mortality in patients undergoing EVAR, compared with patients undergoing open AAA repair (1.7% EVAR *v* 4.7% OR) (Greenhalgh et al, 2004); the DREAM trial reported similar improved 30 day mortality in EVAR versus open AAA patients (1.2% EVAR *v* 4.6% OR) (Prinssen, et al, 2004). The DREAM trial was, however, underpowered, with the result that improved mortality rates did not reach statistical significance. Although the DREAM trial made the point that when combining their results with EVAR 1, the resulting operative mortality of 5.8% for open AAA repair and 1.9% for EVAR, yields a risk ratio of 3.1 (Prinssen, et al, 2004).

Following on from the initial data, during 2005, EVAR 1 and EVAR 2 both published their 4 years mortality data (EVAR trial participants et al, 2005; Prinssen, et al, 2004); EVAR 1 demonstrated that all-cause mortality was similar in the two groups, but that there was a persistent reduction in aneurysm related deaths in the EVAR group (4% *v* 7%). EVAR 2 demonstrated that no benefit was shown in patients undergoing EVAR compared with those receiving "best medical treatment"(EVAR trial participants, 2005). The underpowered DREAM trial has also published further survival data (Marc et al, 2008), but initial (30 day) perioperative survival advantage of EVAR over open AAA repair was not sustained after the first year.

The UK EVAR trial has provided much needed level one evidence for the endovascular repair of abdominal aortic aneurysm. However, the controversy around the patients crossing from different arms and the interpretation of the results raised concerns and debate on its conclusions.

Firstly, for various reasons, only 1082 of 4789 evaluated patients were randomized into this trial. In total, 54% of the patients with AAA were unsuited for EVAR due to their aneurysm anatomical morphology. But only 1.4% patients were unfit for open repair.

This suggests that, regardless of the trial outcome, open repair still played a role for about one-half of patients presenting with larger AAAs (≥ 5.5cm).

The EVAR 1 trial concluded that there was no significant difference in the primary end point of all cause mortality, which was about 28% for both groups, at 4 years. There was also no difference in quality of life (QOL) at 12 months, one of the important secondary end points. But the remaining end points showed significant differences. The most important difference was a 3% advantage for EVAR in aneurysm-related death from short, 30 day mortality (1.7% EVAR v 4.7% OR) and this survival advantage remained at 4 years (26% EVAR v 29% OR).

The EVAR 2 trial enrolled many patients rejected from the EVAR 1 trial because they were unfit for open repair (n = 338). The initial EVAR mortality was high (9%), and 64% of patients died during the 4 years of observation with no significant differences between the two groups. The intent-to-treat analysis found no significant difference in all cause mortality between the two groups (45% EVAR v 40% no intervention). There was also no significant difference in AAA-related death (14% EVAR v 19% no intervention), although there was a cross over in the curve midway, with the trend favouring EVAR. Interventions were higher with EVAR at 46% v 26% for no intervention, and hospital costs were three times higher for the EVAR group (£13,632 EVAR v £4934 no intervention). The trialists concluded that there was no advantage to EVAR over no treatment in patients unfit for open repair. But it needed to point out that there was an excessive delay of 57 days between randomisation and procedure in the EVAR arm, and protocol violations in EVAR 2, because 27% of patients assigned to no treatment crossed over to receive aneurysm repair without clear, valid reasons.14 (80%) died even before receiving EVAR, including 6 AAA ruptures. Another 3 ruptures occurred in the EVAR treated patients. In contrast, the 47 patients who crossed over (35 EVAR, 12 OR) had an operative mortality of only 2% and only about half the mortality at 4 years (23%). In an intent-to-treat analysis, these results are credited to no treatment. These results have raised the suspicion that it biased against EVAR. Furthermore, the trialists found no significant differences in all-cause mortality (P =0.7), and AAA related deaths (P=0.43). But if we eliminate those patients who died before they even received their EVAR treatment, and include those who crossed over to receive a repair, the 31% mortality of those receiving a repair (61/197) is significantly lower than the 45% mortality (57/125) of no intervention.

The results of EVAR 1 and EVAR 2 trials have suggested that EVAR is technically effective and safe, with a lower short-term morbidity and mortality than open repair. But the long-term success of EVAR in preventing aneurysm-related deaths is still uncertain.

Worldwide, in addition to the UK EVAR trial and the Dutch DREAM trial, the French Aneurisme de l'aorte abdominale: Chirurgie versus Endoprothese (ACE) study and the United States Open Versus Endovascular Repair (OVER) study are yet to be published. But, there is a comparative prospective cohort study using administrative data from Medicare beneficiaries in the USA (Lyratzopoulos, et al, 2009). In this study both the open and EVAR patients were followed for 4 years. The perioperative rates of death and complications, long-term survival, rupture, and reinterventions after both methods of repair were compared. The data was propensity-score–matched from 2001 to 2004 and in follow-up until 2005. There were a total of 45,660 patients and 22,830 matched patients in each cohort group. The average age of the patients was 76 years, and approximately 20% were women. The results show that perioperative mortality was lower after EVAR than after open repair (1.2% vs. 4.8%, $P<0.001$), and the reduction in mortality increased with age (2.1% difference for those 67 to 69 years old vs. 8.5% for those 85 years or older, $P<0.001$). Late survival was similar in the two cohorts groups, although the survival curves did not converge until after 3 years. By 4 years, rupture was more likely in the EVAR cohort than in the open-repair cohort (1.8% vs. 0.5%, $P<0.001$), as was reintervention related to abdominal aortic aneurysm (9.0% vs. 1.7%, $P<0.001$), although most reinterventions were minor. In contrast, by 4 years, surgery for laparotomy-related complications was more likely among

patients who had undergone open repair compared with those who had undergone EVAR (9.7% v 4.1%, P<0.001), as was hospitalization without surgery for bowel obstruction or abdominal-wall hernia (14.2% v 8.1%, P<0.001). The author concludes that compared with open repair, EVAR is associated with lower short-term rates of death and complications. The survival advantage is more durable among older patients. Late reinterventions related to abdominal aortic aneurysm are more common after EVAR, but are balanced by an increase in laparotomy-related reinterventions and hospitalizations after open surgery.

2.5. Long-term Results and Future of EVAR

Currently, there is no convincing evidence about the long-term outcome of EVAR. The future of EVAR will no longer need to be held in comparison with conventional open surgery; instead, the focus will be on the improvement of technological design of endovascular prostheses and their delivery systems. The long-term outcome will not just rely on the mechanical but biological durability of endovascular prostheses.

2.6. Recommendations from the National Institute for Health and Clinical Excellence (NICE) in the UK on Asymptomatic, Unruptured, Large (at least 5.5 cm in diameter) Infra-renal AAAs

In the United Kingdom, the National Health Service (NHS) is the main provider for delivery of care for patients with AAA, therefore the position of the NHS towards

EVAR determines whether all endovascular practitioners can continue to offer EVAR to their AAA patients. The NHS is nationally funded, run and controlled by the UK government. It offers free health care for all EU citizens.

2.6.1 **Recommendations**

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation, under the NHS, responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health. NICE has produced guidelines in reference to the use of endovascular stent–grafts or open surgical repair only for the treatment of infrarenal abdominal aortic aneurysms with the following statement (http://www.nice.org.uk):

1: Endovascular stent–grafts are recommended as a treatment option for patients with unruptured infrarenal abdominal aortic aneurysms, for whom surgical intervention (open surgical repair or endovascular aneurysm repair) is considered appropriate.

2: The decision on whether endovascular aneurysm repair is preferred over open surgical repair should be made jointly by the patient and their clinician after assessment of a number of factors including: aneurysm size and morphology, patient age, general life expectancy and fitness for open surgery the short- and long-term benefits and risks of the procedures including aneurysm-related mortality and operative mortality.

3: Endovascular aneurysm repair should only be performed in specialist centres by clinical teams experienced in the management of abdominal aortic aneurysms. The teams should have appropriate expertise in all aspects of patient assessment and the use of endovascular aortic stent–grafts.

4: Endovascular aortic stent–grafts are not recommended for patients with ruptured aneurysms except in the context of research. Given the difficulties of conducting randomized controlled trials, it is recommended that data should be collected through existing registries to enable further research.

In this guideline there are five stent–grafts which are included. These are the Talent stent–graft (Medtronic), Excluder AAA endoprosthesis (WL Gore), Aorfix AAA stent–graft (Lombard Medical), Zenith AAA endovascular graft (Cook Medical) and Endologix Powerlink Systems (Le Maitre). All have been granted Conformité Européene (CE) marking, for use within European Union (EU) countries. Four of the manufacturers stated that their list prices were commercial-in confidence. Lombard Medical stated that the price of their Aorfix AAA stent–graft was £5000, which was a fixed price per patient irrespective of the number of components used. A price to the NHS of £5000 was supported by limited sample data for 2007/08 collected by the NHS Purchasing and Supply Agency from some NHS organisations in England. These data confirmed that the average price of an endovascular stent–graft, irrespective of the number of components used, was £5000.

The NICE guideline has indicated that EVAR is now evidence based medical practice and is an established treatment option to all NHS patients.

2.6.2. Evidence and interpretation of the recommendations

(http://www.nice.org.uk)

The Assessment Group of NICE guideline committee has assessed randomised controlled trials (RCTs) and large registries relevant to UK practice. The registries included were the National Vascular Database (NVD) for open surgery, the Registry of Endovascular Treatment of Abdominal Aortic Aneurysms (RETA) and the European Collaborators on Stent–Graft Techniques for Abdominal Aortic Repair (EUROSTAR). Where appropriate, the Assessment Group used meta-analysis to estimate a summary measure of treatment effect on relevant outcomes, based on intention-to-treat (ITT) analyses.

To identify criteria for selecting patients appropriate for EVAR, the Assessment Group also reviewed studies that modelled a large range of risk factors. Risk-modelling studies were specific to AAA, focused on risk of mortality following EVAR, and used appropriate statistical modelling techniques. Studies were required to be based on a trial, registry or a series of at least 500 patients, from developed countries of relevance to UK practice.

There are four RCTs in EVAR versus OR, comparing EVAR with OR in patients with unruptured AAA (EVAR 1, n=1082; DREAM, n=351; Cuypers and co-workers, n=76; and Soulez and co-workers, n=40). Most patients in the RCTs were men, reflecting the disease profile, and the average age of patients ranged from late 60s to mid-70s. The four RCTs were relatively homogeneous in terms of average aneurysm diameter (6.5cm, 6.0cm, 5.4cm and 5.2cm, respectively).

All four RCTs reported 30-day mortality. The pooled estimate of effect suggested a significantly lower rate of 30-day mortality in the EVAR group: pooled odds ratio (OR) 0.35 (95% confidence interval [CI] 0.19 to 0.63). The 30-day mortality rate of 2.3% in the EUROSTAR registry was comparable with the 1.7% in the EVAR arm of EVAR 1. In the UK NVD crude operative mortality following OR of unruptured aneurysms was 6.8%, compared with 4.7% in the OR arm of EVAR 1.

EVAR 1 and DREAM provided information on all-cause mortality at follow-up (at 4 years and 2 years, respectively). Both RCTs reported no significant difference in medium-term mortality (at 42 and 35 months, respectively) in patients treated with EVAR compared with OR. A pooled analysis of the two trials confirmed there was no statistically significant difference between EVAR and OR, for all-cause mortality at medium-term follow-up.

The four RCTs provided limited information on rupture as a separate outcome. The limited data available suggest that rupture may be more of an issue following

EVAR than following OR. The cumulative rate of rupture in patients from EUROSTAR was 3.1% over 7 years.

Only the EVAR 1 and Soulez and co-workers trials reported endoleak as an outcome. Across these RCTs, some form of endoleak occurred at varying frequencies (up to approximately 20%) following EVAR. Type II endoleaks were most common, followed by type I. The cumulative rate of endoleaks in patients from the EUROSTAR registry was higher (32.5%).

Only EVAR 1 reported on device migration following EVAR. In the trial, 12 of 529 patients (2.3%), experienced device migration during follow-up, of whom seven (1%) required re-intervention.

The EVAR 1 and DREAM trials compared overall re-intervention rates between patients treated with EVAR and OR. In DREAM, the risk of re-intervention was significantly higher in the EVAR group for the first 9 months (hazard ratio 2.9; 95% CI 1.1 to 6.2, p=0.03) but the groups were not significantly different thereafter (hazard ratio 1.1; 95% CI 0.1 to 9.3, p=0.95). At the medium-term follow-up in EVAR 1, the hazard ratio for re-intervention was 2.7 (95% CI 1.8 to 4.1) indicating a higher risk in the EVAR group. The 4-year point estimates for re-intervention in this trial were 20% for the EVAR group compared with 6% for the OR group. The cumulative rate of re-intervention in the EUROSTAR registry was similar to the 4-year point estimate for the EVAR group in EVAR 1.

Only the trial by Cuypers and co-workers reported cardiac events: three (5%) in the EVAR group, and two (11%) in the OR group.

All four RCTs reported some details of health-related quality of life (HRQoL). All used the Medical Outcomes Study short form 36 (SF-36) questionnaire, but different components were reported, making it difficult to compare results across studies. Overall, data from these trials suggested that there may be a short-term quality-of-life advantage for EVAR patients compared with those who have OR. Longer-term quality-of-life data tended to favour OR.

In assessment of EVAR versus non-surgical management, the Assessment Group identified one published RCT (EVAR 2, n=338) that compared EVAR and non-surgical management in patients judged to be unfit for OR. The Assessment Group considered the trial to be of high quality. The primary endpoint was all-cause mortality and secondary endpoints were aneurysm-related mortality, HRQoL, postoperative complications and hospital costs. The trial found no differences in AAA-related and all-cause mortality outcomes between groups at medium term. However, this finding cannot be taken as definitive because substantial numbers of patients randomised to non-surgical management crossed over to receive surgical repair of their aneurysm.

In assessment of risk factors for adverse outcomes following EVAR, the Assessment Group identified 32 studies investigating specific risk factors for adverse outcomes after EVAR. The Assessment Group stated that the studies did

not provide definitive evidence; but age, gender, renal impairment, fitness, American Society of Anesthesiologists (ASA) score, and aneurysm size, may be predictive of lower 30-day survival. There may be an association between fitness for the open procedure, aneurysm size and device type and aneurysm-related mortality. Pulmonary status, renal impairment, ASA score, and aneurysm size might adversely affect all-cause mortality. The Assessment Group did not find any consistent risk factors for re-intervention.

In summary, compared with OR, EVAR reduced operative mortality (OR 0.35; 95% CI 0.19 to 0.73) and aneurysm-related mortality over the medium term (OR 0.49; 95% CI 0.29 to 0.83) but offered no significant difference in all-cause mortality at medium term. EVAR was associated with an increased rate of complications and re-interventions. There was limited RCT evidence comparing EVAR with non-surgical management in patients unfit for OR. Although the EVAR 2 trial found no differences in mortality outcomes between groups this finding should not be taken as definitive.

2.7. Complications of EVAR

The overall complications of EVAR have reduced over the years since its introduction in 1991; in particular, since the newly designed second generation of devices went onto the market in 2001(Van Marrewijk et al, 2005; Curci J A et al, 2007; England A et al, 2008; Hiramoto et al, 2007; Greenberg et al, 2008.).

However, despite the survival benefit in short and midterm, perioperative advantage and general public acceptance of EVAR over open repair, EVAR has more complications than open repair (Hobo, et al, 2006); indeed, this procedure has created a group of complications that are EVAR specific. One of the obvious reasons is that aortic aneurysm is a biological problem and EVAR is merely a mechanical solution. The biological issue around the aortic aneurysm cannot be addressed at the current status of EVAR.

The overall complication rate was reported by the EVAR 1 trial. By 4 years, the proportion of patients with at least one complication following AAA repair was 41% in the EVAR group and 9% in the open repair group. Overall complication rates were 17.6 per 100 person years in the EVAR group and 3.3 per 100 person years in the open repair group, hazard ratio 4.9 (95% CI 3.5, 6.8), $p<0.001$ (EVAR Trial Participants, 2005).

2.7.1 Common technical complications

The common technical complications are listed below:

Stent migration

Stent fracture

Stent wire fracture

Graft stenosis

Type I endoleak

Type II endoleak

Type III endoleak

Type IV endoleak

Endotension

Contrast reaction

2.7.2 Common non-technical complications

The common non-technical complications are listed here:

Cardiac event

Renal impairment

Graft-limb thrombosis

Graft infection

Colonic ischaemia

Lower limb ischaemia

Pulmonary complications

Haemorrhage

Local wound complications

2.7.3 Secondary intervention after EVAR

The rate of secondary intervention after EVAR has been reported by the EUROSTAR Registry (Hobo, et al, 2006). The results show that the annual cumulative rate for secondary intervention was 6%, 8.7%, 12%, and 14% at 1, 2, 3, and 4 years, respectively, resulting in an annual mean secondary intervention rate of 4.6%. This has meant that lifelong surveillance of EVAR patients is necessary. Among the EVAR complications that are specific to the stent-graft, the most

important are endoleak and migration. The details of these complications will be discussed below.

2.7.4 Endoleak

Endoleak is defined as persistence of blood flow outside the lumen of the Endoluminal graft but within the aneurysm sac, as determined by an imaging study (White et al. 1996: White et al. 1997)

Endoleak remains one of the main reasons for the existence of EVAR being challenged. It is one of the technical complications specific to EVAR, and is one of the commonest causes of stent-graft failure. The result of endoleak is lack of complete exclusion of blood flow within the aneurysm sac. It represents the failure in the goal of EVAR. Endoleak may continue to pressurize the aneurysm sac and therefore lead to possible ongoing aneurysm enlargement and rupture. In many respects, the phenomena of endoleak remain unclear. It is vitally important to understand the mechanism of endoleak, so that permanent solutions resolving this phenomenon can become possible.

There are four types of endoleak according to the origin and site:

Type I endoleak (Figure1A) is attachment site leaks. It is perigraft channel of blood flow caused by inadequate or ineffective seal at either the proximal (Type I A) or distal attachment zones (Type IB). In the case of aorto-mono-iliac stent grafts, Type IC endoleak can occur. Type IC endoleak is due to the aneurysm

being reperfused by the nonoccluded iliac artery in patients with aorto-mono-iliac stent and femoral-femoral bypass.

Type II endoleak (Figure 1B) is due to the retrograde filling of the aneurysm sac from its patent branches. This commonly occurs from lumbar arteries and/or IMA, but also in rare situations from sacral, gonadal, accessory renal artery, or internal iliac artery. Some authors have further divided Type II endoleak into Type IIA when they are simple and related to only one patent branch, and Type IIB when they are complex, with 2 or more patent branches (Cao et al, 2010).

Type III endoleak (Figure 1C) are caused by a structural failure of the implanted device, including junctional separation of modular components (Type IIIA), due to migration or changes in vessel morphology with aneurysm shrinkage, holes in the fabric, and fabric tears due to graft strut fracture or erosion (Type IIIB).

Type IV endoleak (Figure 1D) is caused by porosity of the graft fabric. This is seen at the time of device implantation as a faint blush on the post implantation angiogram when patients are fully anticoagulated. This type of endoleak can usually only be detected <30days after graft implant. They are rarely seen with current devices and seal spontaneously.

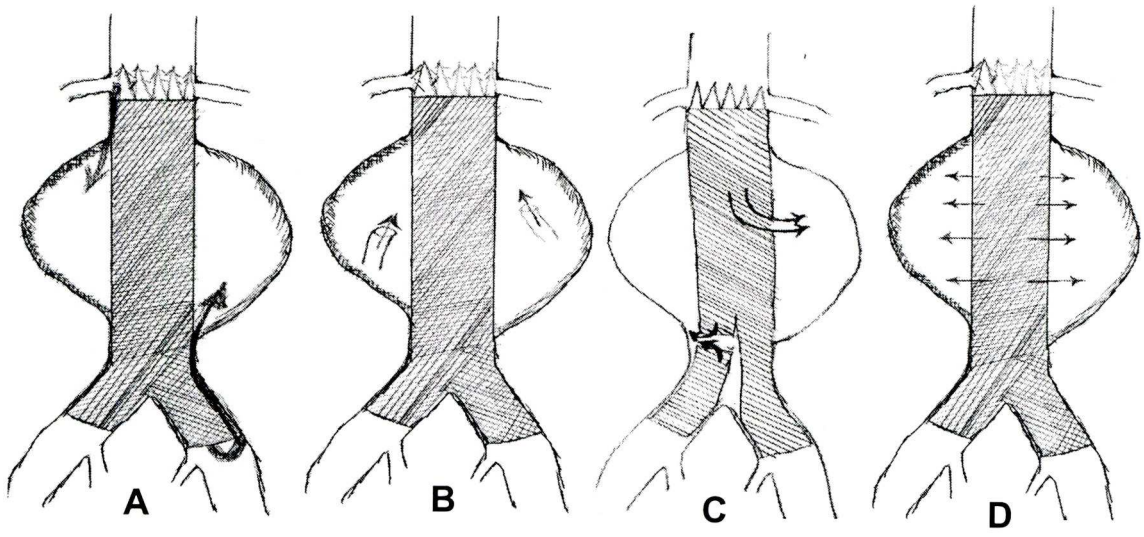

Figure 1: Diagrams to show the four types of endoleaks. Type I endoleak (Figure1A) is perigraft channel of blood flow caused by inadequate or ineffective seal at either the proximal(Type I A) or distal attachment zones (Type IB). Type II endoleak (Figure 1B) is due to the retrograde filling of the aneurysm sac from its patent branches. Type III endoleak (Figure 1C) is caused by a structural failure of the implanted device, including junctional separation of modular components due to migration or changes in vessel morphology with aneurysm shrinkage, holes in the fabric, and fabric tears due to stent strut fracture or erosion. Type IV endoleak (Figure 1D) is caused by porosity of the graft fabric. This is seen at the time of device implantation as a faint blush on the postimplantation angiogram when patients are fully anticoagulated.

Endotension sometimes is referred to as Type V endoleak. It constitutes tension on the aortic aneurysm sac, and has been defined as any rise of intrasac pressure or expansion of the aneurysm after EVAR, that occurs without visualized endoleak on delayed contrast imaging (computed tomography, magnetic resonance) scans. It was first described by Gilling-Smith et al (Gilling-Smith et al, 1999). According to the consensus document (Veith et al, 2002), classification scheme of endoleaks includes a category of endotension without any endoleak, even during open surgical conversion (endotension Type A); and a category with a sealed or clotted endoleak (endotension, Type B). Here, the leak becomes apparent only when a clot is removed from the branch orifice at operation. In addition, patients with a Type I or Type III endoleak may not have leaks visualized on CT or MRI scan but still have a high intrasac pressure (endotension, Type C); similarly, patients with Type II endoleak may not have a visualized leak but still have high intrasac

pressure (endotension, Type D). In these two latter categories, the endoleak becomes apparent only when the aneurysm sac is opened. Whether patients with Type C and Type D endotension behave like those with Type 1, III, or II leaks, respectively, remains to be determined.

Endoleaks can also be classified according to the time of first detection. Perioperative endoleaks occur within 24 hours of endovascular repair of aortic aneurysm; early endoleaks occur between 1 and 90 days after endovascular repair and late endoleaks occur more than 90 days after endovascular repair. Endoleaks can also be described as primary, if they are detected at the time of endovascular repair or secondary if they appear at a later date.

Endoleak remains the most common cause of secondary intervention after EVAR. According to the individual studies that have been reported, the overall incidence of endoleak depends on the device used and the duration of follow up. EUROSTAR data has reviewed 2,463 patients of which 171 (6.9%) had endoleak by the first month postoperative assessment and 317 (12.9%) patients had a new-onset endoleak at later dates. In total, there were 488 (19.8%) patients in whom an endoleak was observed at any time after the endograft implantation. The prevalence of endoleaks during follow-up was approximately 20%.

Type I endoleak is manifestation of sealing failure at one of the attachment sites of the graft to the aortic wall. Type I endoleak is associated with significant pressure

increase in the sac. The perigraft space is therefore under systemic pressure, representing a failure in the treatment of the aneurysm that continues to be pressurized and at risk for continued expansion and rupture (Harris et al, 2000; Buth et al, 2000, Dias et al, 2007).

Incidence of Type I endoleak has been reported to be as high as 10% after EVAR (Veith et al, 2002; van Marrewijk et al, 2002) with 4.2% at 30 days, 3-5% within 1 year and 6.7% beyond 1 year (Wilt et al, 2006).

A Proximal Type I endoleak, in particular, may result in serious consequences if it remains untreated. The results from the EUROSTAR registry have suggested that proximal Type I endoleaks have much higher risks of late conversion (Harris et al 2000; Vallabhaneni et al 2001) and rupture (Marrewijk et al 2002). Also, compared with distal Type I endoleak, the proximal type one endoleak has a significantly higher risk of aneurysm rupture (Mohan et al 2001).

Clinical observation suggests that an aortic neck length less than 15 mm is associated with increased risk of Type IA proximal endoleak (Stanley et al, 2001; Sternbergh et al, 2002; Zarins et al, 2003) and 15-20% of stent-graft proximal attachment oversizing can help to achieve excellent sealing (Cao et al, 2010). Clearly, 15-20% oversizing may not be sufficient for neck length less than 15mm (Stanley et al, 2001; Sternbergh et al, 2002; Zarins et al, 2003). But does the 15-20% "rule" apply to all aortic necks longer than 15 mm? What about the aortic

necks shorter than 15 mm? Should oversizing be increased to achieve excellent sealing? Clearly, insufficient oversizing of a stent-graft will result in incomplete seal with subsequent proximal Type I endoleaks, or inadequate fixation with the potential risk of migration. On the other hand, excessive oversizing may increase the risk of complications, such as stent-graft infolding or dilatation of the aneurysm neck, with subsequent migration and endoleak (Schurink et al 1999; Conners et al 2002; Sternbergh et al 2004). So, it is fair to assume that different aortic neck lengths require different oversizing to achieve excellent sealing. Further study is needed to approve or disapprove this assumption. It is also important to understand the relationship between oversizing and aneurysm neck length. Only then is it possible that an adequate seal can be determined, by optimising the percentage oversizing.

2.7.5 Migration

Migration is described as the longitudinal movement of the stent-graft or attachment system relative to anatomic landmarks or to its original deployment site. However, there is no general agreement as to how far a stent-graft has to move in order for it to be considered to have migrated. So far it has been suggested that the migration distance should be at least 5mm (Lifeline Registry Participants, 2001) or at least 10mm (Ahn et al, 1997; Chaikof et al, 2002; Greenberg et al, 2004).

Stent graft migration is one of the most serious late complications after EVAR (Zarins et al. 2003; 2003; Hobo. et al. 2006). Migration may lead to aneurysm

repressurisation and rupture. It also may lead to stent-graft kinking, thrombosis and lower limb ischaemia.

Migration has occurred in all commercially available stent-grafts (van Marrewijk et al. 2005; Drury et al. 2005), and has been extensively reported in many clinical studies. The reported prevalence of migration was from under 3% to 28% (Tonnessen et al. 2005; Zarins et al. 2003; van Herwaarden et al. 2007). The factors affecting migration were the type of stent-grafts used, aortic aneurysm morphological characteristics and the length of study follow-up time (Tonnessen et al. 2005; Zarins et al. 2003; van Herwaarden et al. 2007). The proximal aortic neck length, diameter and angle seem to have great influence on the risk of proximal stent-graft migration after EVAR. (Tonnessen et al. 2005; Zarins et al, 2003; Fulton et al, 2006; Albertini et al, 2000; Leurs et al, 2005). The other risk factors that have also been studied are maximum aneurysm diameter, stent-graft configuration (aortic tubes, aortomonoiliac, bifurcation grafts), the type of proximal stent-graft fixation (suprarenal / infrarenal, with / without hooks and barbs) and the extent of stent-graft oversizing (Sternbergh III et al. 2004; Waasdorp et al. 2005; Mohan et al 2002; Leurs et al.2005; Faries et al.2002; Resch et al.2000).

Clinical studies into the relationship between proximal oversizing and graft migration have produced conflicting results. Some studies suggest there is no significant association between oversizing and migration (Sampaio et al, 2005; Cao. et al, 2002).

There are experimental studies investigating the relationship between oversizing and the required force for stent-graft displacement. Malina et al. used cadaveric aortas to measure the longitudinal distraction that was required to dislodge Zenith-stents from the aorta (Malina et al, 1998). This study suggested that stent-graft oversizing had no effect or only slightly increased the required force for displacement of stent-grafts with or without barbs, respectively. However, the limitation of this study was that the percentage of oversizing was not accurately determined, the aorta was not pressurized as it would be in vivo, and the exact mode of migration was not described.

Experimental, and some clinical data suggest that the adequate proximal fixation strength is the most important factor to prevent stent-graft migration. However, clinical studies have produced conflicting and even confusing results regarding whether oversizing plays any role in creating adequate fixation strength (van Prehna et al, 2009). Migration is a recognised and acknowledged complication, but the mechanism is still unclear. So there is clearly a need for further studies to investigate the exact mechanisms of migration and the effect of oversizing on migration.

When a stent-graft is implanted, it will be subject to forces due to the effect of pulsatile blood pressure and blood flow, both of which can produce longitudinal haemodynamic force. This force will tend to constantly push the stent-graft down-stream from its proximal attachment site. To resist these forces and prevent migration, the implanted stent-graft needs to have sufficient fixation strength.

The longitudinal haemodynamic force exerted on stent-grafts *in vivo* has been estimated previously using analytical mathematical models (Liffman et al. 2001, Mohan et al, 2002, Morris et al. 2004). Mohan et al showed that hypertension, aneurysm geometry and iliac angulation, amongst other factors, were significantly associated with stent-graft migration. These findings were validated using a simple one-dimensional analytical model based on momentum equation, not accounting for the pulsatility of blood flow and the viscosity of the fluid. It was shown that under certain conditions, the longitudinal force (LF) on a stent-graft due to blood flow and pressure may exceed the fixation force causing stent-graft migration. Since the analytical models neglect the effects of blood viscosity and the pulsatility of blood flow and blood pressure, further studies are needed to determine whether or not these parameters significantly affect the longitudinal haemodynamic force acting on the bifurcated stent-graft.

2.8. Summary

Endovascular aneurysm repair is by now a well-established treatment concept that has dramatically changed the overall approach to AAA repair. With the improvement in stent-graft design and more clinical experience gained, the complications of EVAR have fallen significantly in recent years. The benefits of endovascular repair for the large abdominal aortic aneurysm (>5.5cm), in short and midterm, are less controversial. However, due to lack of predictive preclinical scientific research, most of the improvements in stent-graft performance resulted

from the findings of clinical observation. EVAR is associated with its own unique problems after implantation and those problems are largely not understood. Endoleak and stent-graft migration are the two most significant complications leading to failure of EVAR. It is vitally important to understand these two phenomena so the future design of the stent-graft can be improved upon. The long term durability of EVAR will continue to be challenged as long as these two complications remain unresolved.

CHAPTER 3

FENESTRATED ENDOVASCULAR ABDOMINAL AORTIC ANEURYSM REPAIR (FEVAR)

3.1. Introduction

Standard EVAR has become an established alternative to open surgical treatment of abdominal aortic aneurysm. However, anatomical limitations for standard EVAR have precluded its application to all infrarenal aortic aneurysms. The main reason for the ineligibility for standard EVAR is short aortic neck length. A study suggests that 55% patients were considered suitable for EVAR and 45% patients deemed ineligible. The most common anatomical reason for ineligibility was a short infrarenal neck (44%) (Arko et al 2004). Similarly, Carpenter et al reported short aneurysm neck accounts for up to 54% of all causes for ineligibility for standard EVAR (Carpenter et al, 2001).

Many studies of conventional commercial aortic stent-grafts have demonstrated that short or compromised proximal aortic necks can lead to inadequate proximal seal thereby increasing the risk of proximal endoleak, device migration, and aneurysm rupture (Hovsepian et al, 2001; Morrisey et al, 2002; Mohan et al, 2002). These results have led to a generally accepted anatomic requirement for a proximal neck length of 15 mm for most commercially available stent-grafts for EVAR.

It has been well studied that the operative mortality and morbidity rates associated with elective open repair of AAA with short aortic neck length are higher than for standard infrarenal aneurysm (Jean-Claude et al 1999; Sarac et al 2002; West et al 2006). To reduce the operative mortality and morbidity rates in open repair, a minimal invasive endovascular treatment is needed to treat this group of patients.

As this group of patients has short or compromised proximal aortic necks, the covered sealing stent has to be placed above the orifices of the renal, and possibly the superior mesenteric (SMA) and coeliac arteries to secure the proximal seal. Fenestrated endovascular aneurysm repair (FEVAR) offers a solution in this situation.

Fenestrated stent-graft is an extension of the application of EVAR. It was designed to overcome the limitation of short infrarenal neck length in aortic aneurysm repair. With the fenestrated technique, it was estimated that about 80% of infrarenal aortic aneurysms could be treated with an endovascular approach (Carpenter et al, 2001).

With fenestrated EVAR, the fenestrated stent-graft is placed proximal to the side branches thereby providing a good length for the sealing zone. Since the side branches are intentionally covered, it is necessary to provide fenestrations in order to restore perfusion through the use of stents (Figure 3.1).

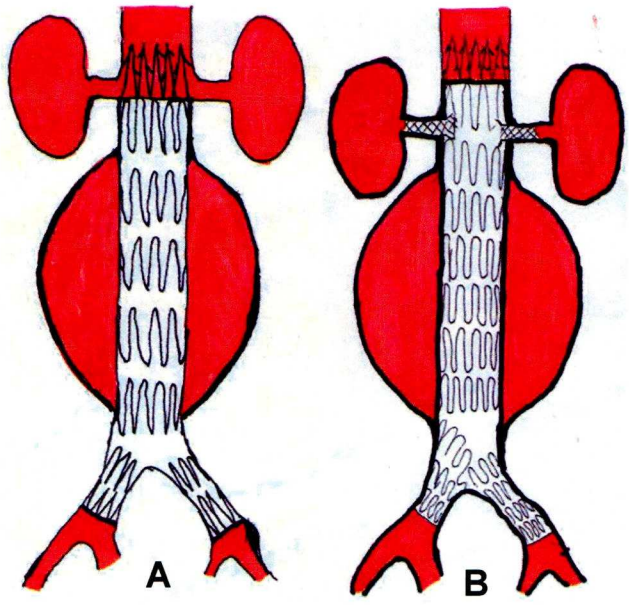

Figure3.1: This is a diagram to show the difference in proximal landing zone between the conventional (A) and fenestrated (B) EVAR.

3.2. Development and Configuration of Fenestrated EVAR

Fenestrated aortic grafts were first described in 1996, in 2 patients with infrarenal aortic aneurysms (Park et al, 1996). Development and clinical utilization of these grafts was led by Lawrence-Brown and associates (Browne et al 1999).

A fenestrated stent-graft is a composite device based on the Zenith system (Cook, Brisbane, Australia), which has a self-expanding modular design with an uncovered Gianturco Z-stent (Cook Europe, Bjaeverskov, Denmark) for proximal fixation in the standard configuration (Figure 3.2A). It consists of a straight tubular proximal portion, a bifurcated distal portion and a contralateral iliac limb. The proximal part of the graft is fitted with diameter reducing ties to allow only partial deployment prior to catheterization of the side branches and final orientation of the stent-graft (Figure 3.2 A-C)

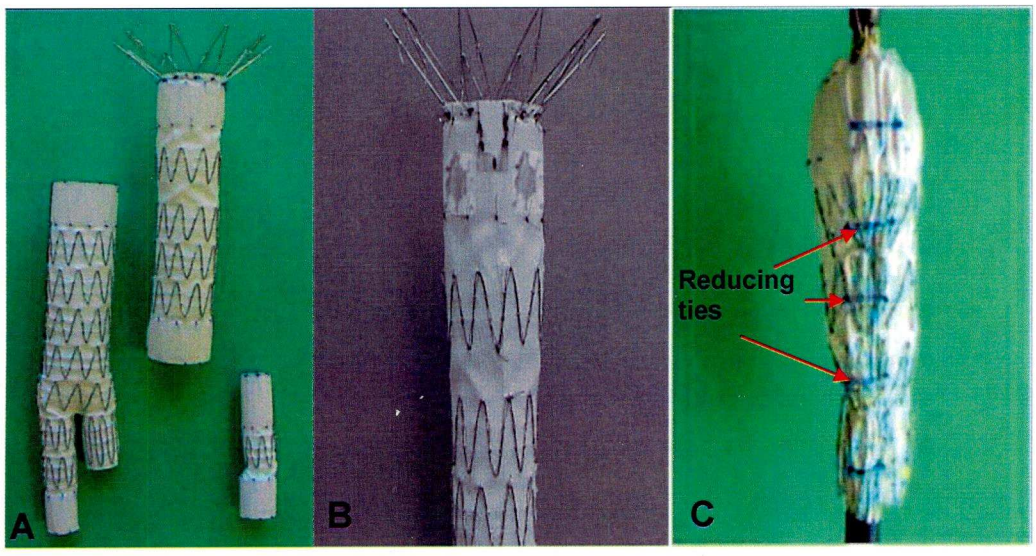

Figure3.2: Picture of fenestrated stent-graft, (A) components of composite body, the proximal portion of stent-graft with two small fenestrations (B) and partially deployed proximal portion of graft with reducing ties (C).

A fenestrated stent-graft is custom designed and manufactured according to individual anatomy incorporating accurately placed holes in the stent-graft that align with renal/visceral vessel ostia. Stents are placed through the fenestrations. There are three types of possible fenestrations: scallops, large and small fenestrations (Figure 3.3 A-C). Each fenestration is marked by 3 (for scallop) or 4 (for a small or large fenestration) radiopaque markers to enable accurate alignment. Each tube graft is fitted with anterior and posterior markers to facilitate orientation during insertion and deployment.

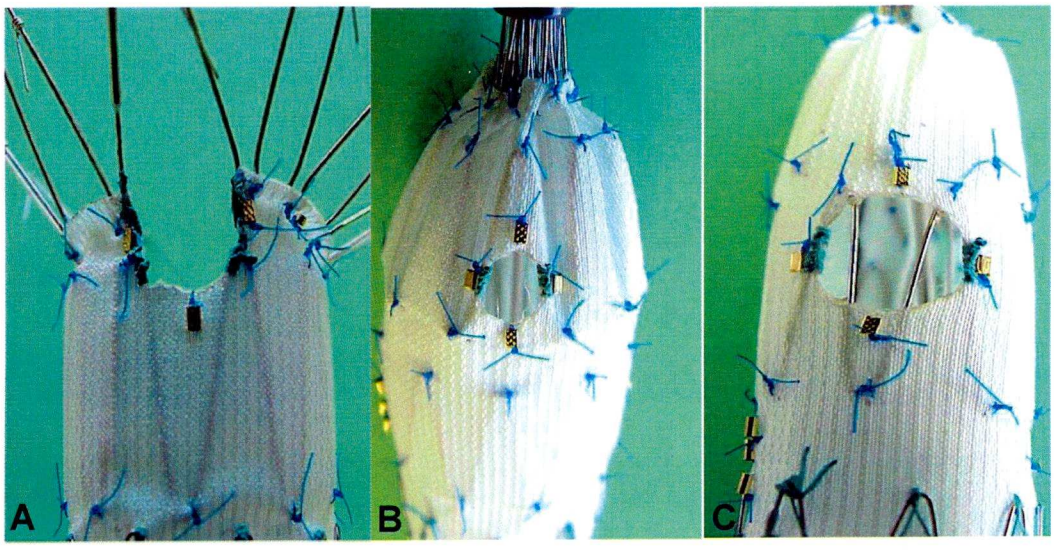

Figure 3.3: Pictures to show the three types of fenestration. Scallop (A), small fenestration (B) and large fenestration (C).

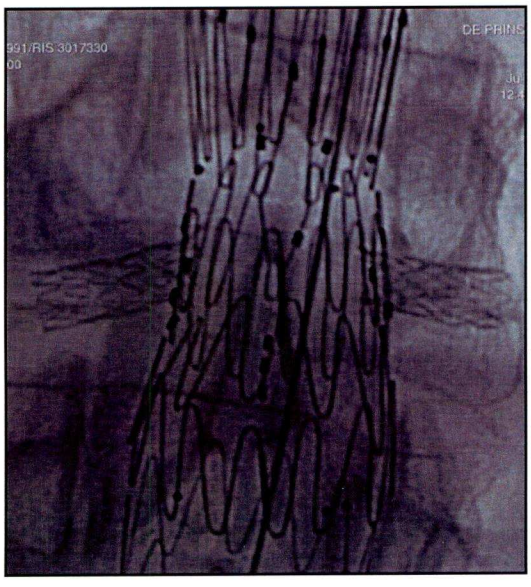

Figure 3.4: This is a plain abdominal x ray to show two small fenestrations with stents.

A further evolution in design of the fenestrated device is to reinforce fenestrations and scallops with nitinol rings (Figure 3.5). The reason for this is to hold the fenestration and scallop open for catheterization in the middle stages of deployment when the body of the stent-graft is still in a partially compressed state.

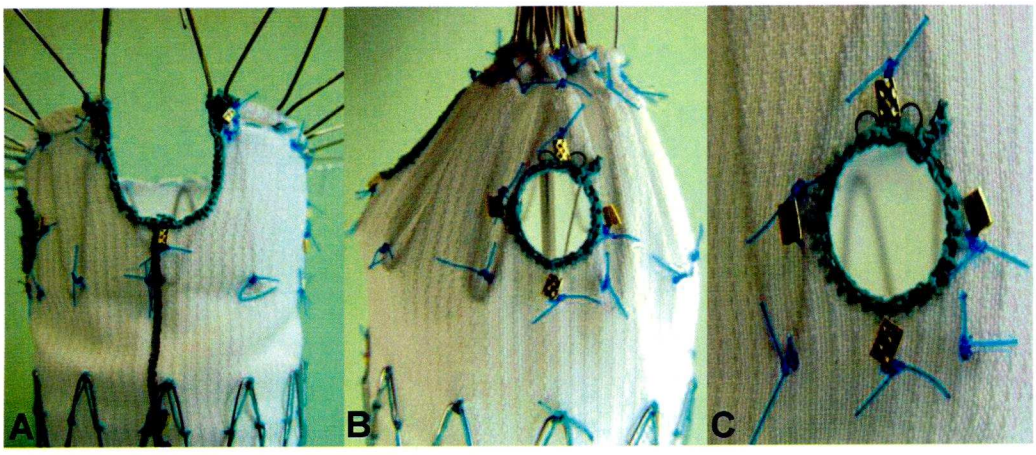

Figure 3.5: Photographs of fenestrations reinforced with Nitinol rings.

3.3 Indication and Planning for Fenestrated EVAR

The indications for fenestrated EVAR vary according to individual institutions, but there appears to be a general acceptance that aneurysms with diameter above 5.5cm and short, hostile aortic neck are suitable for fenestrated EVAR.

Planning and deployment of Fenestrated EVAR are technically more challenging than for standard EVAR. It requires advanced catheter skills and much more training when compared with standard EVAR. The approach is also different in dealing with late secondary interventions. Planning a fenestrated stent-graft requires detailed analysis of aortic anatomy, in particular the proximal landing zone. The information required includes the diameter of the aorta at the level of the target vessels, the orientation of each target vessel along the circumference of the aortic cross section, orthogonal separation between the different target vessels and the desired size of each fenestration. The configuration and orientation of each vessel should also be studied to plan a strategy for the operation.

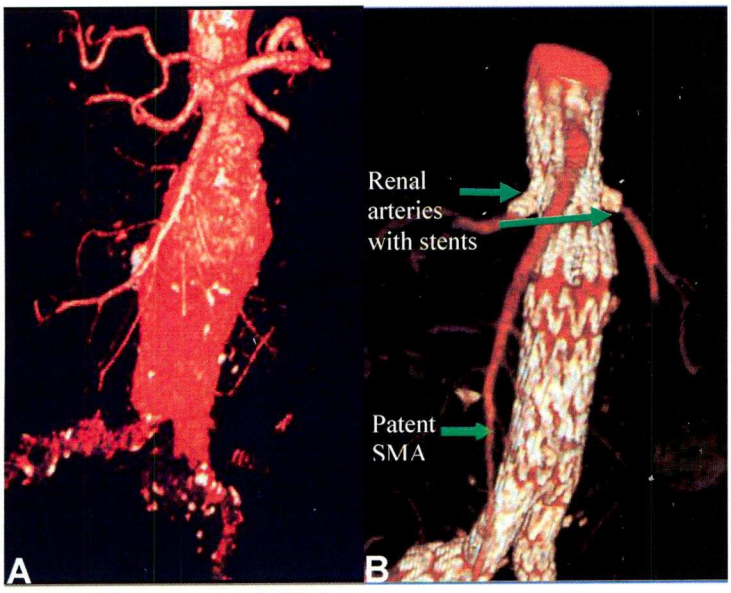

Figure 3.6: Three-dimensional computed tomographic reconstructions of a juxtarenal abdominal aortic aneurysm (A) before and (B) after fenestrated endovascular aneurysm repair.

3.4. Short and Midterm Outcomes of Fenestrated EVAR

Since the initial report in 1996 (Park et al, 1996), fenestrated EVAR devices have been implanted in over 1,500 patients worldwide (O'Neill et al, 2006) and are now commercially available (Kristmundsson et al, 2009) to all centres that have the necessary technical skills and equipment to perform this procedure. Since most of the published results are from single centre series, it is difficult to make comparable results.

3.4.1 Mortality

Reported mortality from individual institutions ranged from less than 1% to more than 2%. Cumulative mortality following fenestrated EVAR was 1.4% (Nordon 2009). Causes of mortality included mesenteric ischaemia (Muhs et al, 2006;

O'Neill et al, 2006) and myocardial infarction (MI) (Semmens et al 2006; Scurr et al 2008) with no intraoperative deaths.

3.4.2 Renal impairment

An overall perioperative renal impairment rate of 14.9% (CI 11.5-18.7) has been reported. However, most of these were early, transient renal failures which completely recovered. About 1.4% of patients required permanent dialysis from renal failure (Anderson et al 2001; Halak et al 2006; Muhs et al 2006; O'Neill et al 2006; Ziegler et al 2007; Scurr et al 2008; Bicknell et al 2009).

3.4.3 Primary endoleak

Primary Type I and III endoleaks represent a failure to completely exclude the aneurysm. The reported Type I or Type III endoleak rate was 6.9% at immediate postprocedural imaging. These were managed by additional Palmaz stenting, balloon expandable stenting or conservative observation. Not all studies have reported Type II endoleak, although it may be of less clinical significance (Halak et al 2006; Muhs et al 2006; O'Neill, Semmens et al 2006; Ziegler et al 2007; Scurr et al 2008; Bicknell et al 2009).

3.4.4 Target vessel patency

Target vessel patency is a measure of primary technical success and fenestrated EVAR stability. All the studies have reported primary technical branch fenestration success, and most reported target vessel patency. At follow-up, 96.6% of target vessels were preserved within the perioperative period (in hospital and within 30 days post-surgery). In the studies with median follow-up more than 1 year, one-year patency had reduced to 92%. In this period, no patient developed new

dialysis- dependent renal failure (Halak et al 2006; Muhs et al 2006; O'Neill Semmens et al 2006; Ziegler et al 2007; Scurr et al 2008; Bicknell et al 2009;).

3.4.5 Secondary re-intervention

Most studies reported re-intervention after fenestrated EVAR was by endovascular means, apart from laparotomy for ischaemic viscera. The indications for secondary re-interventions included endoleaks, complications with access vessels and surgical excision of ischaemic viscera. The reported re-intervention rate in the first year following fenestrated stent-graft deployment was 15% with range 0-24%. Nearly half of cases (48%) were for endoleaks (Type I 21%, Type II 8%, Type III 19%). The remaining half of cases (52%) were angioplasty of visceral or peripheral vessel stenoses, access and wound vessel complications and laparotomy for mesenteric ischaemia (Halak et al 2006; Muhs et al 2006; O'Neill Semmens et al 2006; Ziegler et al 2007; Scurr et al 2008; Bicknell et al 2009).

3.5 Unresolved issues in fenestrated EVAR

Since migration has occurred in all commercially available stent-grafts (van Marrewijk et al 2005; Drury et al 2005), it is not surprising that it can also happen in fenestrated EVAR.

In fenestrated EVAR, patency of target vessels (vessels whose perfusion is preserved via the fenestrations or scallops) remains a source of concern in the short and the long term. Stent-graft movement of less than 5mm may not cause concern in the majority of standard stent-grafts. However, with a fenestrated stent-graft, migration of even this magnitude can result in distribution of shear forces to the interface between the target vessel stent and the fenestrated body of the stent-

graft. Their hoop strength may not be sufficient to withstand these forces, resulting in crushing or even fracture of stents and possible occlusion. It remains unknown whether the hoop strength of the fenestration stent can increase the overall proximal fixation strength.

Stents that are usually placed into target vessels were not primarily designed to withstand high levels of asymmetric stress. However, it is not clear whether their presences across the proximal main body of the device can affect the overall fixation strength of the insitu stent-graft.

A fenestrated stent-graft is designed to treat the infrarenal aortic aneurysm with a short infrarenal neck length. However, it is not certain what minimum infrarenal neck length is required to achieve a secure seal in fenestrated EVAR, whether bare stents should be used up to a certain length of aortic neck, or covered stents should be used in all cases. In addition, what degree of optimal oversizing is required for secure seal in fenestrated EVAR remains undefined.

CHAPTER 4

RATIONALE AND SUMMARY OF INVESIGATIONS

The aim of endovascular repair of aortic aneurysm (EVAR) is to permanently exclude the blood flow and pressure to the aneurysm wall, therefore eliminating the risk of aneurysm rupture.

Proximal Type I endoleak and migration of endovascular stent-graft are the two commonest and most important causes of failure after EVAR (Harris et al, 2000; Vallabhaneni et al 2000; Marrewijk et al 2002; Zarins et al 2003; Hobo. et al. 2006).

The aim of oversizing is to achieve an adequate proximal seal. However, the long term security of the seal is reliant on the graft's proximal fixation against migration.

There are many factors which can influence the tendency for endovascular stent-graft migration, such as morphological features of the aortic aneurysm, the characteristics of the selected endovascular stent-graft, and the downstream force created by the longitudinal haemodynamic force.

In clinical practice, there remains controversy over the effect of oversizing on migration (van Prehn et al; 2009). The hypothesis is that stent-graft oversizing has a significant effect on the proximal fixation strength, and the maximum effect is reached at a certain percentage of oversizing; beyond which, further oversizing will

not bring any further benefits. Stent-grafts with fixation bare stents and barbs have higher fixation strength than those without (Chapter 6).

Fenestrated EVAR is designed for infrarenal aortic aneurysms with a short neck. The purpose of stenting the branch vessels are to retain their patency, but a secondary result of branch vessel stenting may be an increase in the overall stent-graft fixation strength. Stent-graft migration is frequently observed in clinical practice, but the mode of migration was not known before. The hypothesis is that standard and fenestrated stent-graft migration occurs in phases (Chapter 7). The fenestrated stent-graft configuration confers greater proximal fixation strength than conventional devices (Chapter 7).

The aim of stent-graft oversizing is to obtain an effective seal. It is not necessary and can be risky to excessively oversize the aortic neck beyond the optimal degree of oversizing requirement. It is also unknown whether the same degree of oversize is needed for different aortic neck lengths. The hypothesis is that the optimal degree of oversizing is aneurysm aortic neck length dependent; the shorter the neck length, the greater the degree of oversizing needed for an effective seal (Chapter 8).

The longitudinal haemodynamic force (LF) is a downstream dragging force, created by blood flow. The fixation strength of any commercially available stent-graft should therefore exceed the LF acting on it- to safeguard against migration.

The LF exerted on stent-grafts *in vivo*. has been estimated previously using mathematical models (Liffman et al. 2001, Mohan et al, 2002, Morris et al. 2004).

However, these findings were only validated in a simple one-dimensional analytical model based on momentum equation, not accounting for the pulsatility of blood flow, and the viscosity of the fluid. The hypothesis was that under certain conditions, the LF on a stent-graft due to blood flow and pressure may exceed the fixation force, thus causing stent-graft migration (Chapter 9).

CHAPTER 5

Experimental Methodologies

5.1 Introduction

In this chapter the methodologies adopted in the experiments to: 1) investigate the relationship between optimal oversizing and proximal fixation strength, 2) compare the fixation strength of standard and fenestrated stent-grafts and 3) investigate the optimal oversizing required for an effective seal in standard and fenestrated EVAR, 4) measure the longitudinal haemodynamic force in a bifurcated stent-graft model, are described. The results of these experiments are presented in Chapters 6, 7, 8 and 9, respectively.

The abdominal portions of fresh bovine aortas were obtained, and all adherent non-vascular tissue removed. For the experiments with fenestrated stent-graft, larger branches (5–6 mm wide when pressurized) were identified for stenting. A length of at least 3cm was provided to accommodate the stent. For the experiments with standard stent-graft, marks were made at 3.0cm intervals along

the length of the aortic segment as measurement points. All the measurements were taken at those measurement points.

We pressurised the freshly prepared bovine aorta with normal saline, so the aortic diameter could be changed by changing the applied pressure. In all our experiments, the aortic internal diameter was used and it was calculated through external diameter and volume of aortic wall in any particular segment.

After insertion of the proximal portion of stent-graft, the oversizing of stent-graft over aorta could then be accurately determined by changing the pressure applied to the aorta.

Zenith stent-grafts were used in all experiments with barbs and the proximal bare stent was removed for experiments without barbs. Since all experiments were concerned with proximal fixation or seal, the stent-grafts were truncated leaving only the proximal portion. In experiments with fenestrated stent-graft, a single 6mm fenestrated stent-graft was constructed. The fenestrations were not reinforced. The stent-grafts were sealed and tested for waterproof for the experiment of oversizing and seal.

To investigate the optimal oversizing required to achieve adequate proximal fixation strength, force was applied to the stent-graft to cause it to migrate within the aorta, the peak force was recorded and analysed. In comparison of the fixation strength of standard and fenestrated stent-grafts, a fenestrated stent-graft

was constructed, and the force to cause it to migrate was compared with that for a standard stent-graft. The same methods were used in creating accurate oversizing and force measurement.

In the experiments to investigate the optimal oversizing required for an effective seal in standard and fenestrated EVAR, the same methods were used to determine the stent-graft oversizing. Standard and fenestrated stent-grafts were initially sealed to waterproof and then partially deployed into bovine aorta at an appropriate site at certain length and then connected to a purpose built system which could generate pulsatile flow. The system can mimic human infrarenal blood flow. The pressure and flow settings were generated from elderly patient blood pressure and infrarenal blood flow. Fluid of the same viscosity as normal human blood serum was used. The system was connected to a computer for controlling and monitoring pressure and flow. Any leak between the aorta and the stent-graft was observed.

To measure the longitudinal haemodynamic force acting on the stent-graft, a bifurcated stent-graft model was machined, using aluminium tubes joined with metal-loaded epoxy resin, to form a bifurcation. The main trunk internal diameter was 30 mm, and wall thickness was 4 mm. We thinned a segment 30 mm long to 0.1 mm wall thickness on the main trunk. The thinned segment increased the level of strains locally, so that the strain could be easily measured. Two strain gauges were bonded onto this section. After calibrating the strain gauges, the model was placed onto the same pulsatile flow system. The longitudinal haemodynamic force was then measured and converted to Newtons.

5.2 Experimental Methodologies of Investigating the Relationship Between the Optimal Oversizing and Proximal Fixation Strength and Comparison of the Fixation Strength of Standard and Fenestrated Stent-graft for EVAR in Chapters 6 and 7.

5.2.1 Development and designs of experimental methods of measurement of displacement force in relation to stent-graft oversizing

The experiment was initially designed to place the bovine aorta in an upright position. After the aorta was sealed and pressurised with saline, known weights were placed on the stent-graft through a connecting system. After a test run of over 20 tests, we found that the results were not reliable and repeated experiments could not produce the same results. This was due to the columnar pressure from the saline adding extra pressure inside the aortic lumen and creating uneven intraluminal pressure. Furthermore, this pressure kept changing, with changing aortic internal diameter. As the results of this, we changed the position of the aorta from upright to horizontal, replaced the weights to a calibrated digital force gauge and placed onto a linear drive to make sure the force applied onto the stent-graft was linear.

The bench top experiment (Figure 5.1) for the measurement of distraction force comprised a pressurised bovine aorta into which the proximal portion of a standard or fenestrated Zenith stent-graft (Cook Europe, Bjaeverskov, Denmark) was deployed. Force was applied to the stent-graft to cause it to migrate within the aorta, under observation; this displacement force was measured with a calibrated digital force gauge. Since the experiment in chapter 6 was to determine the relationship between the oversizing and proximal displacement force (the force

required to displace the stent-graft), a wide range of oversizing was used (5%, 10%, 20% 30%, 40% and 50%).

In chapter 7 however, the aim was to discover the mode of displacement and to compare the displacement force between the fenestrated and standard stent-graft, and so oversizings of 5%, 10%, and 20% were used.

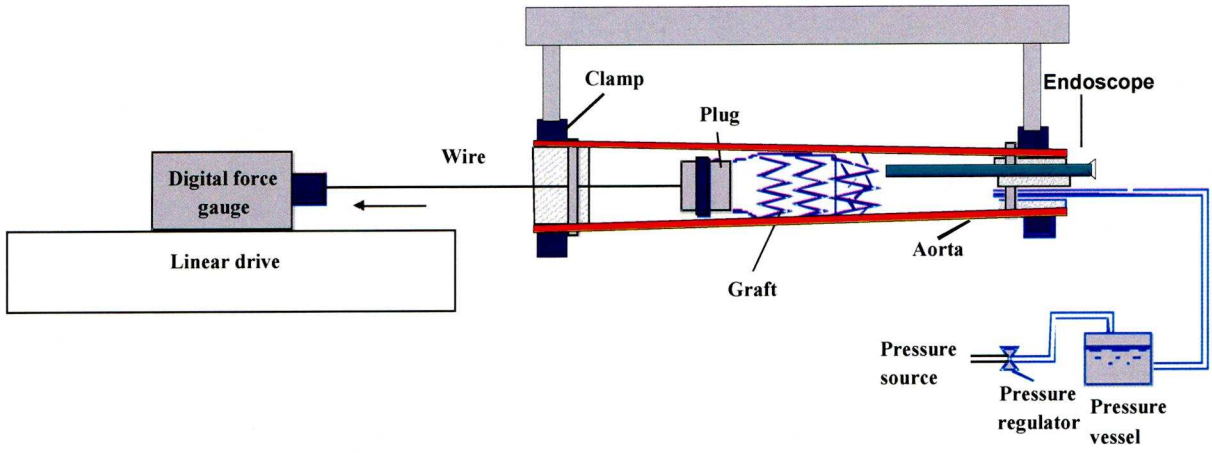

Figure 5.1: Diagram of experimental set up

5.2.2 Selection and preparation of the aortic specimens

Conducting this experiment with human cadaver infrarenal aorta would be the ideal Use of human aortic tissue would have been the obvious first choice. However, since there is legislation in place regarding obtaining human tissue for scientific research in United Kingdom, it has proven that any application for such purposes is extremely complicated, and approval takes at least two years on average. This would have been impossible for us.

The second choice would be using porcine aorta, but the problem with that is since foot and mouth disease, all the older pigs' tissue is destroyed for safety, and only the younger pigs' tissue can be obtained. After measurement of younger pig's aorta, we found that porcine aorta has a much smaller size for the available Zenith stent-graft to produce any meaningful oversize.

Finally, fresh bovine aorta was used and obtained from an abattoir, after a pressure test run, we found that the bovine aorta can sustain much higher pressure without compromise to its integrity, it is compliant and can produce reliable diameter change, under repeated pressures.

The abdominal portion was retained and all adherent non-vascular tissue, removed. For the experiments with fenestrated stent-graft, larger branches (5–6 mm wide when pressurized) were identified for stenting. A length of at least 3cm was provided to accommodate the stent. For the experiments with standard stent-graft, marks were made as measurement points at 3.0cm intervals along the length of the aortic segment. All the measurements were taken at the measurement points (Figure 5.2).

Figure 5.2: Prepared bovine aorta for the experiments with fenestrated stent-graft (A) and standard stent-graft (B).

Any leaking areas were oversewn using 4–0 Vicryl sutures. The aortas were stored in normal saline at 4°C for a maximum of 24 hours after preparation, during which the experiments were conducted.

5.2.3 Stent-graft oversizing

The "oversizing" was created by changing the aortic luminal pressure. Thus the internal diameter of aorta at the measurement point was changed. By altering the luminal pressure, the appropriate internal diameter was determined for the desired oversizing. Initially, we placed the aorta vertically. After sealing both ends of the aorta, known weights were placed at the distal end of the aorta and pressure applied. We soon found out that the results of the measured aortic external diameter were not accurate and not reproducible; this was clearly due to the difference of columnar pressure from the intraluminal fluid at different measurement points. To avoid this error, we placed the aorta horizontally, so the pressure at all measurement points remained the same. However, another

problem was observed; when the aorta was pressurized, this not only increased its diameter, but also its length; and the higher the pressure, the longer the aorta became. As a result, the aorta became slack, so it made it impossible to measure any linear fixation force along its lumen. To avoid this problem, we fixed both ends of the aorta at the highest intraluminal pressure range, to keep the aorta straight at all times.

After correcting the above problems, we then determined the internal diameter of the pressurized bovine aorta from the relationship of the internal diameter to pressure over the range 60 to 160 mmHg for the experiments in chapter 6. In this pressure range, there were far fewer sites with branches suited for fenestration, with desired oversizing. Therefore in chapter 7, we increased the pressure range from 60 to 190 mmHg, so that we could recruit more sites for the experiments with fenestrated stent-graft. For the experiments with standard stent-graft, the interval between the measurement points was 3.0 cm along the length of the aortic segment. The wall thickness at each axial location was measured using digital callipers. The aorta was then plugged at both ends, and the lumen was pressurized with saline to a pressure of 160 mmHg for the study in chapter 6, and 190 mmHg for chapter 7. The length of the aortic segment at this pressure was measured. The ends of the aorta were then securely clamped so that the length of the aorta remained constant during the experiment. The external diameters of the aorta over the range 60 to 160, or 190 mmHg pressure were determined at each marked location using the digital callipers (Figures 5.3 & 5.4).

Figure 5.3: Picture of external diameter measurement of a bovine aorta.

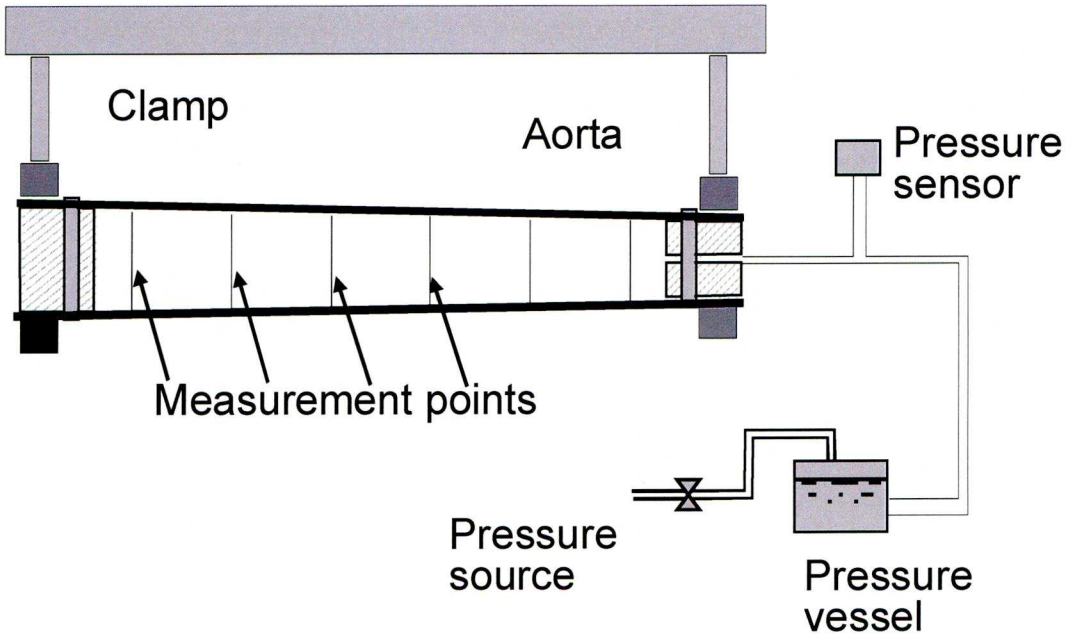

Figure 5.4: This is a diagram to show the experiment of aortic diameter-pressure relationship study set up.

From known external diameter at the measurement points, the respective internal diameter can be calculated, through the differences between the external and internal columnar volumes.

As we know, to calculate the volume (V) of any given circular column structure, when diameter (D) and length (L) are known, the volume (V) is given as

$$V = \pi L(\frac{D}{2})^2 \qquad \text{(Equation 5.1)}$$

Although the bovine aorta was tapered over its full length, each 3cm segment between the marks was considered to be a straight tube, whose diameter was the average of the proximal and distal end diameters of that particular segment (Figure 5.4). So, the total external luminal volume of a particular segment of length L, proximal external diameter D_{po}, and distal external diameter D_{do} can be calculated as

$$V = \pi L(\frac{Dp_o + Dd_o}{4})^2 \qquad \text{(Equation 5.2)}$$

Similarly, the intraluminal volume of the particular segment of length L, proximal internal diameter D_{pi}, and distal internal diameter D_{di} can be calculated as follows:

$$V = \pi L(\frac{Dp_i + Dd_i}{4})^2 \qquad \text{(Equation 5.3)}$$

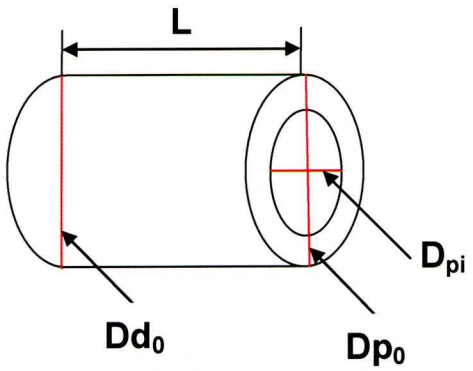

Figure 5.5: This is a diagram to explain how the internal diameters were calculated.

Assuming that the volume of the aortic wall remains constant at any luminal pressure, the internal diameter can be calculated from the external diameter. The volume V of the aortic wall is represented by the formula

$$V = \pi L\left[\left(\frac{Dp_o + Dd_o}{4}\right)^2 - \left(\frac{Dp_i + Dd_i}{4}\right)^2\right] \qquad \text{(Equation 5.4)}$$

For convenience and easier understanding, the formula can be expressed as the following

$$V = \frac{\pi L}{4}\left[\left(\frac{Dp_o + Dd_o}{2}\right)^2 - \left(\frac{Dp_i + Dd_i}{2}\right)^2\right] \qquad \text{(Equation 5.5)}$$

The subscript *o* denotes external, and subscript *i*, the internal dimensions. Knowing the external diameter D_o, the internal diameter can then be calculated by the following formula:

$$Di = \sqrt{D_o - \frac{4V}{\pi L}} \qquad \text{(Equation 5.6)}$$

Once the relationship between the luminal pressure and the internal diameter of the aorta was determined, it was possible to establish the segment in the aorta wherein a stent-graft of a certain diameter should be deployed, as well as the pressure that should be applied to achieve a known oversizing.

5.2.4 Stent-graft construction and deployment

Zenith stent-grafts (Cook Europe, Bjaeverskov, Denmark) have a proximal bare stent with fixation barbs located midway along alternate stent struts. This stainless steel stent segment is fixed to the main trunk of the stent-graft with monofilament sutures. Stent-grafts of 28, 30, and 32 mm nominal diameter were deployed within different aortic segments under appropriate pressure to achieve the desired degree of oversizing. We kept the bare stent intact for the experiments with barbs; and removed the bare stent for the experiments without barbs.

Since the study in chapter 6 aimed to measure the proximal fixation strength with relatively short necks, all stent-grafts were truncated within the main body at 36 mm from the fabric edge, with the first internal stents intact, but removing the second stent from the fabric graft. The actual contact length between stent-graft and the aorta was 17 mm. All stent-grafts were crimped using a noose to introduce them into the aorta; and deployed at the predetermined site, under direct vision (Figure 5.6).

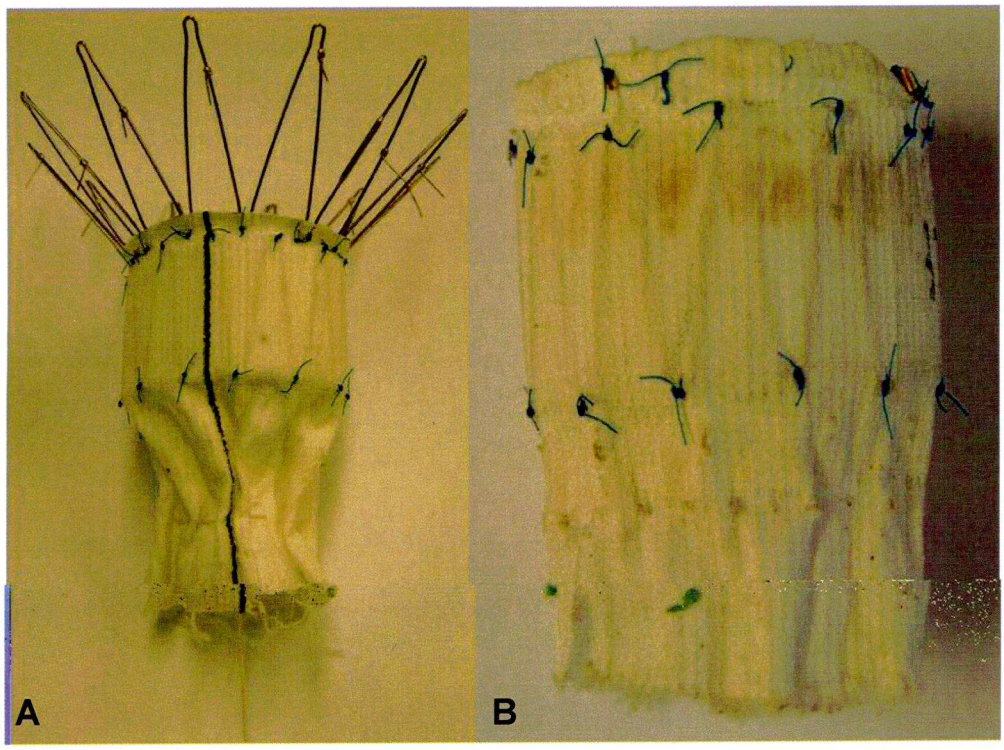

Figure 5.6: Truncated stent-graft with barbs (A) and without barbs (B). The main body at 36 mm from the fabric edge, with the first internal stent intact, but removing the second stent from the fabric graft. The actual contact length between stent-graft and the aorta was 17 mm.

Similarly, for the experiment in chapter 7, all stent-grafts were truncated within the main body. Fenestrated stent-grafts were constructed with a single 6 mm-wide fenestration at a distance of 21 mm from the fabric edge (Fig. 5.7 B). The fenestrations were not reinforced. Since the study aimed to compare the proximal fixation strength between the fenestrated and standard stent-graft, all stent-grafts were truncated within the main body at the same length of 53 mm from the fabric edge leaving the bare stent and the first 2 internal stents intact but removing the third external stent from the fabric graft (Fig. 5.7 A). The actual contact length between both stent-graft types and the aorta was 36 mm.

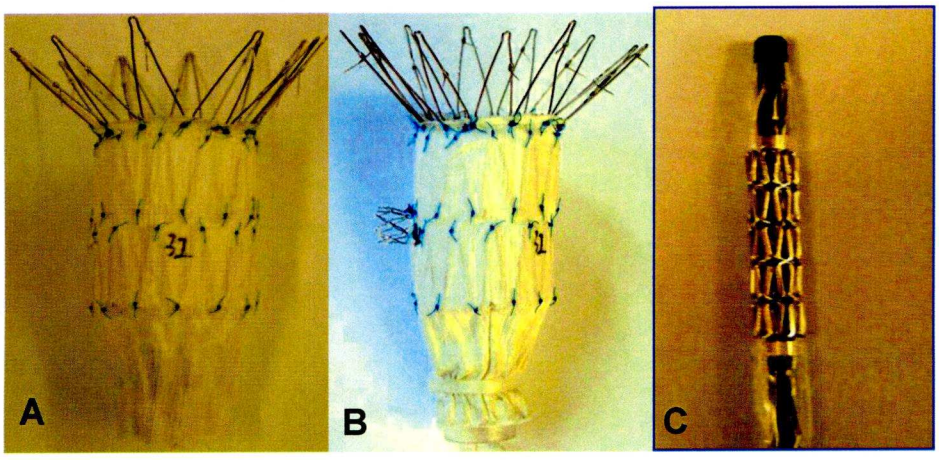

Figure 5.7: (A) Standard, (B) Fenestrated stent-grafts and a 6mm AVE stent (C). All stent-grafts were truncated within the main body at the same length of 53 mm from the fabric edge leaving the bare stent and the first 2 internal stents intact but removing the third external stent from the fabric graft. The actual contact length between both stent-graft types and the aorta was 36 mm. Fenestrated stent-grafts were constructed with a single 6 mm-wide fenestration at a distance of 21 mm from the fabric edge. The fenestrations were not reinforced.

All stent-grafts were compressed using a noose to introduce them into the aorta and deployed at the predetermined site, under direct vision. The fenestrated stent-graft was deployed to align the fenestration with the ostium of a selected side branch with an external diameter of 5 mm. A 6×20 mm balloon-expandable bare stent (Figure 5.6C) (Medtronic AVE, Santa Rose, CA, USA) was placed, under direct vision, through the fenestration, into the side branch and deployed; the stent was then flared with a 12 mm angioplasty balloon.

Because of the natural taper of the bovine aorta, the vessel was reversed in the experiments so that the stent-graft was made to migrate from the narrow segment to the wide segment. Hence, the bare stent was oriented toward the narrower segment of aorta, which was sealed at the end using an internal plastic plug and external gasket arrangement. This plug contained a Luer connection for controlled pressurization of the aortic lumen and also a port to introduce a rigid endoscope (for observing stent-graft behaviour during the experiment). The caudal or unstented portion of the graft was connected to a 0.46 mm diameter stainless steel

wire with a 16 mm diameter plastic plug, which was narrower than the aortic lumen to ensure that only the proximal portion of the stent-graft was in contact with the aorta. The wire was then brought to the exterior of the aorta through a hole in another plastic plug that sealed the end of the aorta toward the caudal end of the stent-graft. This hole contained an O-ring seal to allow free linear movement of the wire, while being leak-proof. The wire was connected to a digital force gauge (Model FG-5000; RS Components, Corby, UK) mounted securely on the moving stage of a manual linear drive, operated by the turn of a wheel. Clockwise rotation of the wheel caused the stage to move to the left, thereby exerting a force on the stent-graft, which was continuously displayed on the force gauge. This gauge was equipped with a "peak-hold" facility to preserve the highest reading should a sudden drop occur in the force being measured. The force gauge was calibrated with known weights, and the maximum deviation was found to be ± 0.05 N.

Once the aorta was pressurized to the predetermined level, the linear drive was engaged, and any slack within the connecting wire was removed. A flag was placed on the wire to facilitate ready identification and measurement of any stent-graft movement. The hand wheel was then rotated slowly whilst continuously recording the distraction force. The stent-graft behaviour during this period was observed through the endoscope.

Each segment of aorta was used only once to avoid errors due to potential mechanical damage of the aorta during the experiment. Stent-grafts were reused only when free from deformation on visual inspection, including the alignment of

fixation barbs. Stent-grafts were also reused only once, to avoid potential errors due to metal fatigue and unidentified deformation. Results were grouped according to the degree of oversizing for standard and fenestrated stent-grafts.

5.2.5 Statistical analysis

The data were presented as the mean displacement force (m-DF) and standard deviation (SD). The force was measured in Newtons (N). They were all represented by a normal distribution of the values within the population. One-way Anova with multiple comparisons (with Bonferroni correction) was used for linear trend regression analysis and to compare the m-DF at different oversizing.

Two-way Anova repeated measurements were used to compare differences in m-DF between the groups with and without hooks. Significant difference was defined as $P< \text{ or } = 0.05$.

5.3 Experimental Methodologies of the Study to Identify Optimal stent-graft oversizing in chapter 8:

Chapter 8 was designed to identify the optimal stent-graft oversizing to achieve an effective proximal seal at different aortic neck lengths, in a pulsatile fluid system.

5.3.1 Experimental Design

The in-vitro model (Figures 5.8 & 5.9) consisted of a sealed, truncated stent-graft which was deployed into the pre-determined measurement point of the bovine aortic section. In a fenestrated stent-graft, a 6 mm AVE stent was used to insert through

the fenestration, into a side branch of the bovine aorta. A purpose built system generated pulsatile flow, mimicking infrarenal aortic flow. It consisted of a piston pump (self assembled) to provide pulsatile flow, and a gear pump (HG 0024 Micro pump INC, Vancouver, WA, USA), to provide steady flow. 40% glycerol solution with physiological viscosity was used as circulating fluid. A pressure sensor and an ultrasonic flow meter (Transonic HT107/HT207 Medical Flowmeter, Ithaca, NY 14850 USA) measured pressure and flow continuously during the experiment. The system was connected to a computer for controlling and monitoring the pressure and flow.

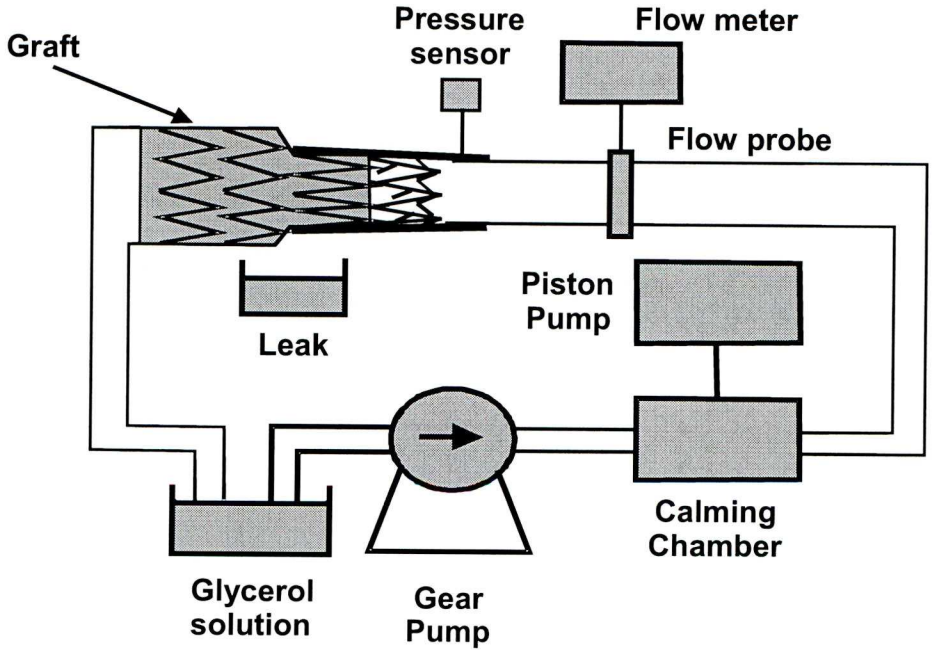

Figure 5.8: Diagram of experimental set up

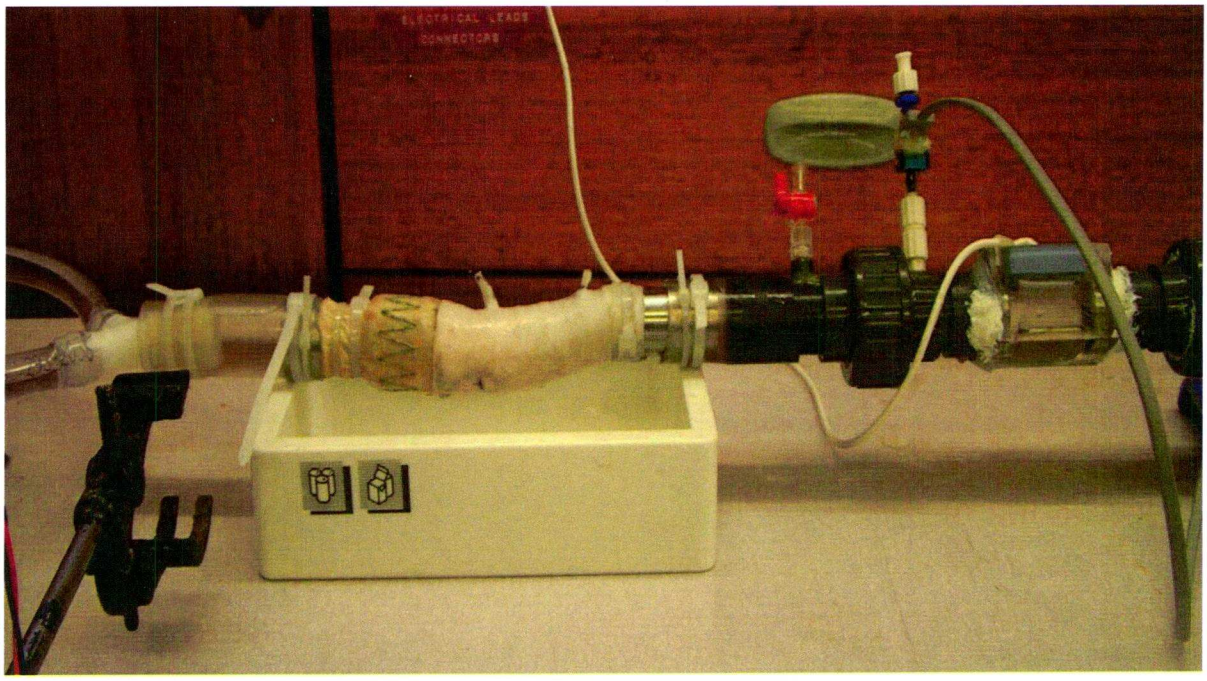

Figure 5.9: Fenestrated stent-graft was deployed into the bovine aorta and connected to the pulsatile flow circuit.

5.3.2 Tissue preparation and stent-graft oversizing

The aortas were prepared using the same method as described in section 5.2.2 and 5.2.3.

5.3.3 Stent-graft construction and sealing

Stent-grafts (Zenith, COOK Europe, Bjaereskov, DK) of 32 mm diameter were used in this study. Since this study considered proximal seal, only the main trunk was used. Each stent-graft was truncated to a fabric covered stent length of 60 mm (figure. 5.10A). Fenestrated stent-grafts (Cook Europe, Bjaeverskov, Denmark) were constructed with a single 6 mm-wide fenestration at a distance of 21 mm from the fabric edge (figure 5.10B). The 6 mm AVE stent (bare stent) was used (figure 5.10C). The fenestrations were not reinforced. As for the standard stent-grafts, each stent-graft was truncated to a fabric covered length of 60 mm.

Then the stent-grafts were sealed with 15% gelatine solution and cross-linked with 1% glutaraldehyde solution to secure the coating. The stent-graft was then pressurized with normal saline at static pressure ranging from 60 mmHg to 190 mmHg, to make sure the seal was water-tight.

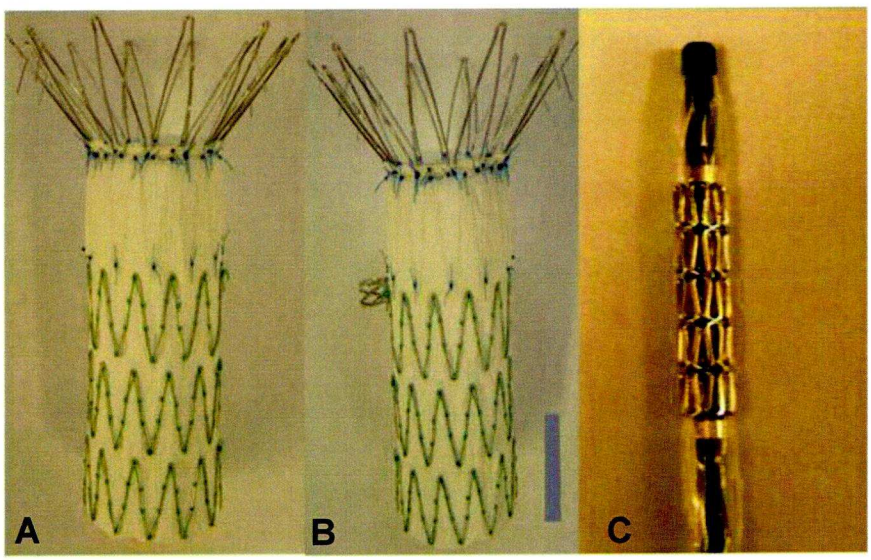

Figure 5.10: Picture of constructed standard (A), fenestrated stent-grafts (B), and 6 mm AVE stent (C).

5.3.4 Definitions of parameter settings

"Endoleak" was defined as any leak between the stent-graft and aorta, observed over five minutes, in each experimental setting.

"Optimal oversizing" was defined as the minimal degree of oversizing at the point at which an effective seal was achieved; -just before the "endoleak" occurs.

"Aortic seal zone length" was defined as the overlapping area between the aorta and the fabric covered stent-graft length. We set the seal zone length at 10 mm, 15 mm, 20 mm, 30 mm and 40 mm for experiments with standard stent-graft and 5 mm, 10 mm, 15 mm and 20 mm with fenestrated stent-graft (Figure 5.11).

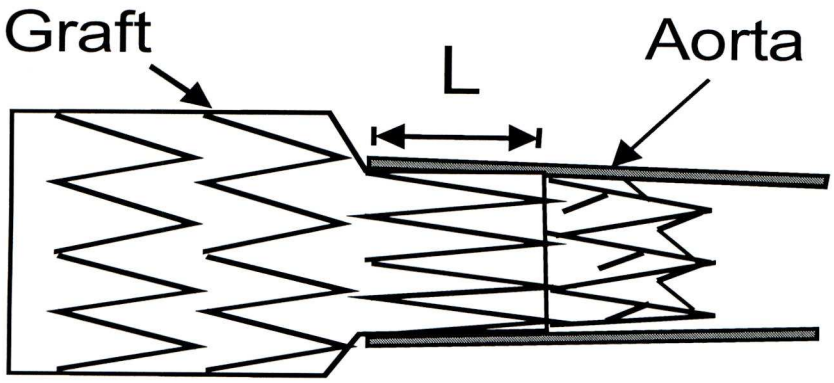

Figure 5.11: Diagram to explain the definition of seal zone length (L).

"Oversize" was defined as a function of stent-graft diameter as shown below (Figure 5.12).

$$Oversize(\%) = (\frac{D}{Di} - 1)X100.$$

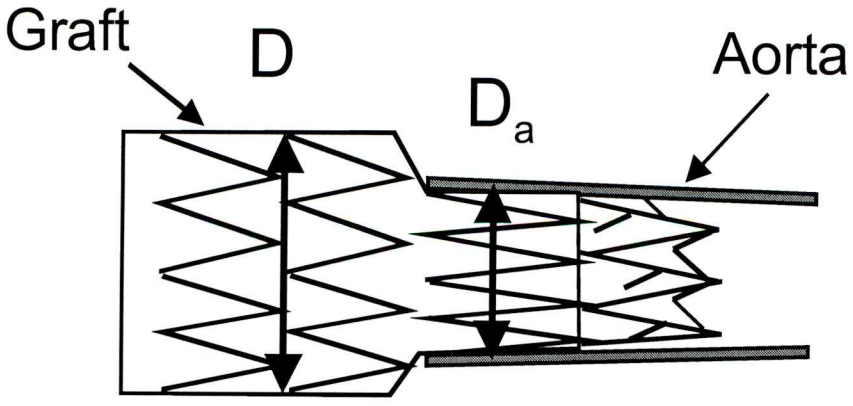

Figure 5.12: diagram to explain the definition of stent-graft oversize.
The percentage oversize ranged from 4% to 26%.

The mean flow rate (1.5 L/min) and flow waveform (Figure 5.13) was taken from normal human subject infrarenal aortic blood flow waveform on duplex scan.

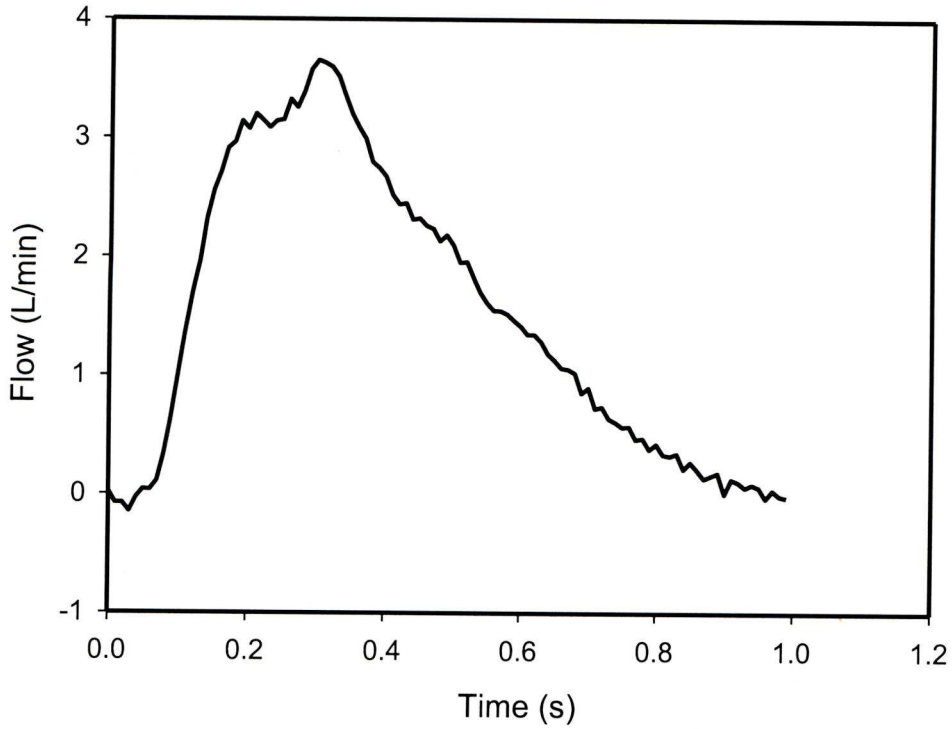

Figure 5.13: Flow waveform was taken from normal human subject infrarenal aortic blood flow waveform on duplex scan.

The pulsatile pressure range was set at "diastolic" pressure from 46 mmHg to 92 mmHg and "systolic" pressure from 60 mmHg to 190 mmHg. The pressure waveform also represented the normal human subject blood pressure waveform (Figure 5.14)

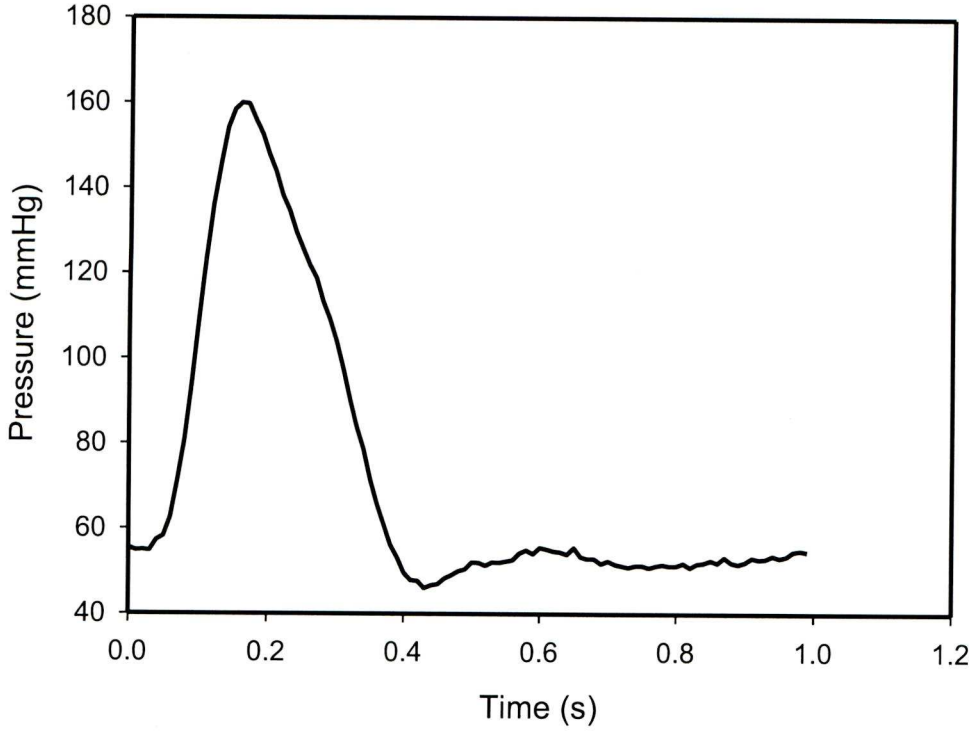

Figure 5.14: Pressure waveform represents normal human subject blood pressure waveform.

The frequency of the pulsatile flow was set to 60 beats/min, representing normal heart rate.

5.3.5 Protocol of the experiment

The stent-graft and aorta were placed in the system. From the aortic pressure diameter study we know, the aortic internal diameter is a function of aortic internal pressure. Therefore the oversize will be different at diastolic and systolic pressures. Maximum oversize occurs at diastolic pressure and minimum oversize at systolic pressure. We started with lowest possible systolic and diastolic pressure, by gradually increasing the pressures, the corresponding oversizing was reduced until leaks between the aorta and the stent-graft occurred. The systolic pressures at the points just before and after leak occurred were recorded so their

corresponding oversizings are known from the pressure-diameter relationship study. The experiment lasted five minutes at each setting, and was repeated a minimum of three times.

In order to determine whether pressure alone can cause leak, we conducted a separate experiment in the same pulsatile flow system. Similarly, we deployed a truncated stent-graft into a bovine aorta and covered the aorta with a rigid sleeve to eliminate oversize variation. We set the seal zone length at 20 mm, oversize at 20% and the pulsatile pressure in the range of diastolic pressure from 60 mmHg to 128 mmHg and systolic pressure from 167 mmHg to 235 mmHg. The experiment lasted five minutes at each setting, and was repeated three times.

5.4 Experimental Methodologies of the Study to Measure the Longitudinal Haemodynamic Force in a Bifurcated Stent-graft Model in Chapter 9

5.4.1 Introduction

The purpose of the study in chapter 9 was to develop an experimental method to measure the longitudinal haemodynamic force (LF) in a bifurcated model of a stent-graft under pulsatile flow of a viscous fluid, and compare the experimental data with the analytical predictions.

In this experiment, we placed a bifurcated stent-graft model into a purpose built pulsatile flow system; any LF exerted on the model could be detected and measured.

The model was machined using aluminium tube, joined with metal-loaded epoxy resin to form a bifurcation. The main trunk internal diameter was 30mm, and wall

thickness, 4 mm. We thinned a segment 30 mm long to 0.1 mm wall thickness on the main trunk. The thinned segment increased the level of strains locally, so that the strain could be easily measured. Two strain gauges were bonded onto this section. After calibrating the strain gauges, the model was placed onto the same pulsatile flow system. The longitudinal haemodynamic force was then measured and converted to Newtons.

The pulsatile flow system could mimic human infrarenal blood flow. The pressure and flow settings were generated from elderly patient blood pressure and infrarenal blood flow.

The viscosity of the viscous fluid was the same as that of normal human blood serum, so the potential effect of viscosity of flow could be eliminated.

5.4.2 Stent-graft material selection

Selection of the correct material to make the stent-graft model was a key factor in the success of the experiment.

One requirement for the material is that it should be able to produce the same strain each time it is under the same stress with no hysteresis; that is, the material should be elastic and stable. Another requirement is that the strain should be easily measured using strain gauges.

We initially selected acrylic tube of 30 mm diameter and measured its tensile strength to see whether acrylic is a reliable material to reproduce the same strain when under the same stress.

The results showed that acrylic material has significant hysteresis. The hysteresis range is from 6.09% to 14.2%. It is not suited for our experiments.

One of the test results are shown in Figure 5.15.

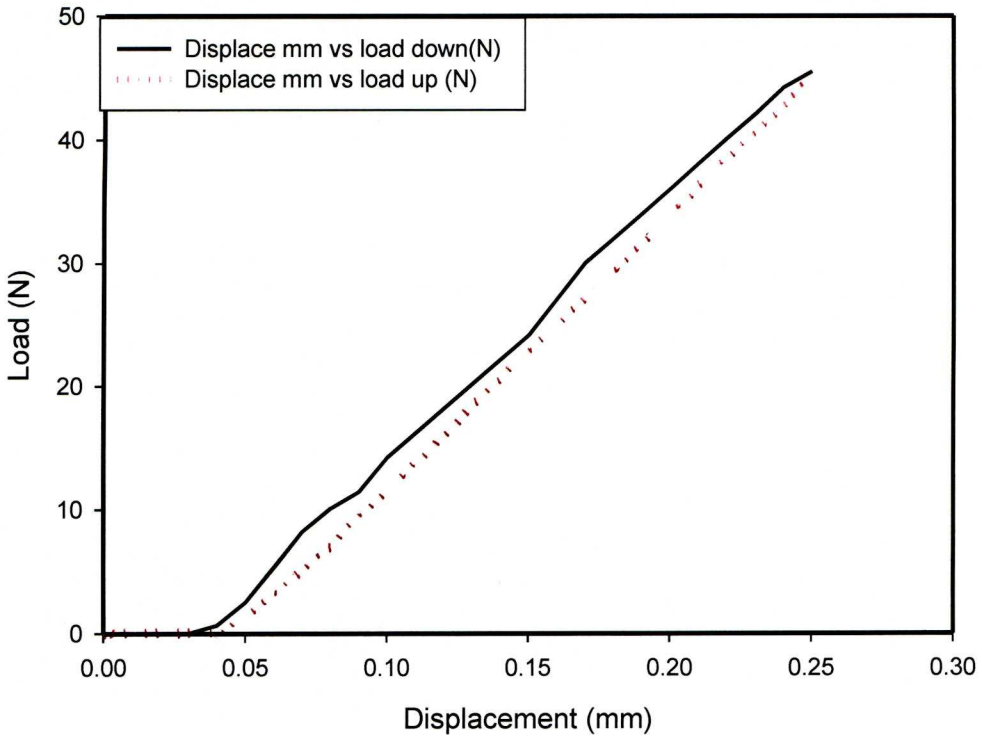

Figure 5.15: One of the test results of tensile strength.

5.4.3 Aluminium stent-graft model

Following the unfavourable results from the acrylic tube, aluminium was selected for the experiments.

The model was machined from aluminium tubes joined with metal-loaded epoxy resin to form a bifurcation. The actual bifurcation was constructed from a bifurcated graft. The main trunk internal diameter was 30 mm, and wall thickness was 4 mm. We thinned a segment 30 mm long to 0.1 mm wall thickness (Figure

5.16). The thinned segment increased the level of strains locally, so the strain could be easily measured.

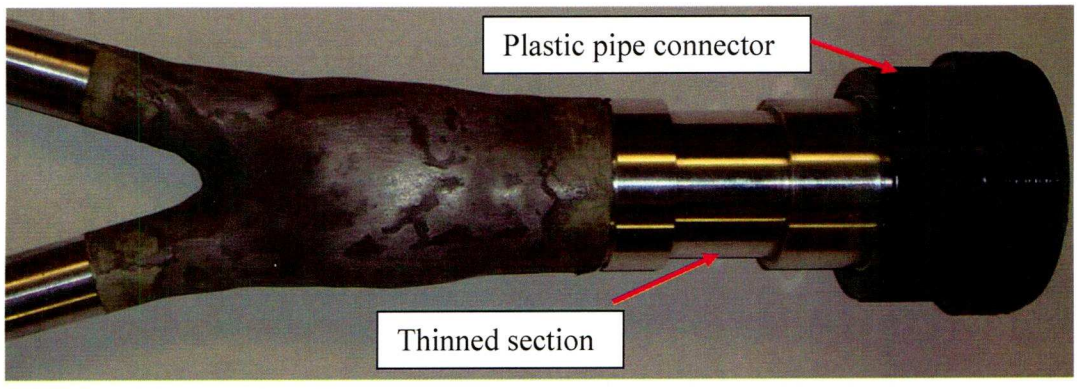

Figure 5.16: Aluminium model of bifurcated stent-graft showing the thinned section. It is provided with plastic pipe connector of the same internal diameter as that of the aluminium tube in order to facilitate connection to the flow circuit.

Two strain gauges (CEA-13-250UN-350, Vishay Micro-Measurements, Reading, UK) from the same batch were bonded onto the thinned section using cyanoacrylate glue (M-Bond 60, Vishay Micro-Measurements, Reading, UK). These gauges are 10.54 mm long by 3.05mm wide and they were placed so that their long axis was parallel to the longitudinal axis of the main cylindrical section. As the model is fixed at its proximal end, the force f_x will result in a longitudinal strain that can be determined by means of the strain gauges. The strain gauges were connected in a half-bridge configuration and two 350Ω high stability precision resistors (S-350-01, Vishay Micro-Measurements, Reading, UK) were used to complete the Wheatstone bridge (Figure 5.17). To minimise the effect of self-heating of the strain gauges, a relatively low dc bridge supply voltage of 2.5 V, provided by voltage reference (LM4140BCM-2.5, RS, Corby UK) was selected. Figure 5.17 shows a photograph of the instrumented stent-graft model.

Figure 5.17: Picture of strain gauges bonded on the model. The two 350Ω bridge completion resistors are also shown.

5.4.4 Measurement of longitudinal Haemodynamic force in an instrumented model of a bifurcated stent-graft

The main body of the stent-graft is subjected to the net longitudinal force $f_{x,}$ which includes the pressure force in the main trunk in the direction of the flow and the iliac limbs in the opposite direction to the flow, and the force due to the momentum change (Figure 5.17). In this case, since a viscous fluid is used, f_x will also include a viscous drag force. This longitudinal force f_x will cause a proportional longitudinal strain in the model (as a result causing the model to elongate), which can be measured. In order to facilitate recording of the strain, the model was thinned locally, as shown in Figure 5.16, thereby increasing the strain level. The graft model was instrumented by means of strain gauges bonded onto the external surfaces of the thinned portion of the cylindrical segment.

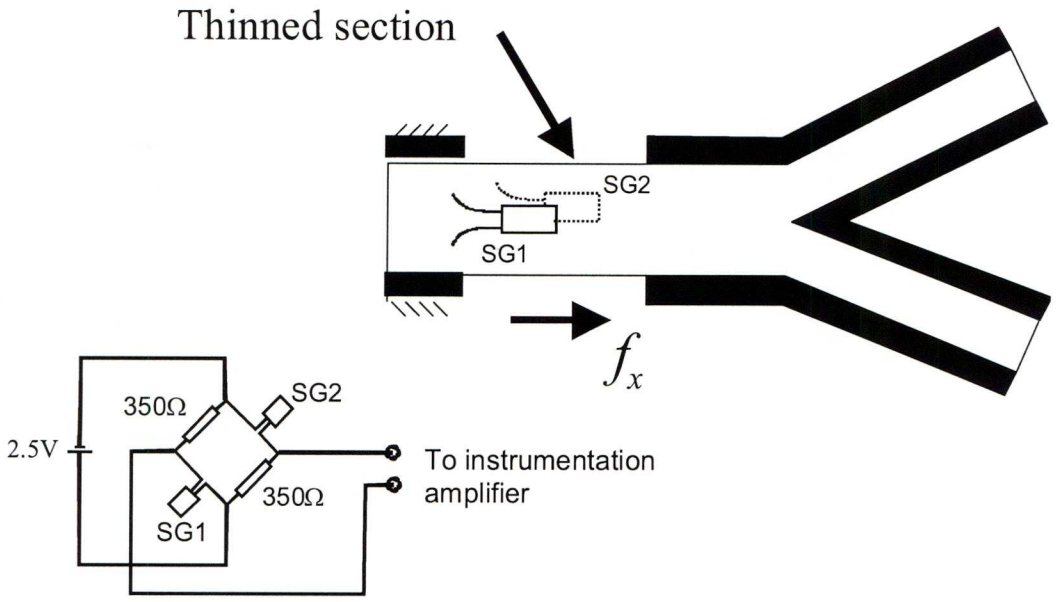

Figure 5.18: Strain gauges were bonded onto opposite sides of the thinned section of the stent-graft model. The proximal section of the model was fixed and the force f_x caused a longitudinal strain which could be measured by means of the strain gauges. The Wheatstone bridge circuit at the bottom shows the connection of the two active strain gauges and the fixed resistors.

5.4.5 Strain Gauge amplifier

The outputs from the strain gauges were fed to a custom-built amplifier, based on a single-chip integrated circuit instrumentation amplifier (INA128, Texas Instrument, RS Corby UK). This amplifier was chosen because it is simple to use and its gain G, can be set by selecting a single resistor Rg according to the formula (Equation 5.9):

$$G = 1 + \frac{50\text{k}\Omega}{\text{Rg}}$$

The complete instrumentation amplifier circuit including the bridge voltage supply is shown in Figure 5.19.

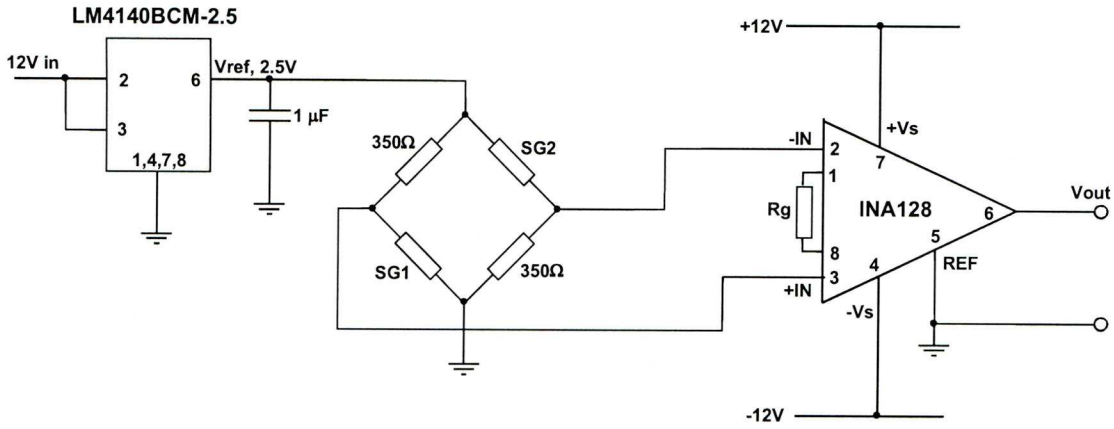

Figure 5.19: Diagram of the signal conditioning circuit, consisting of 2.5V Wheatstone bridge supply and instrumentation amplifier. The output voltage Vout = $G(V_{+IN} - V_{-IN})$

5.4.6 Calibration of the stent-graft model

When a force is applied on the model, a strain, predominantly on the thinned section, will be produced. This strain will be detected by the strain gauges and after amplification, the strain gauges' output will be expressed as voltage. In order to determine the relationship between the force applied and the output voltage, a calibration procedure was used. A series of known weights, from 50 g to 1 kg (at increments of 50 g), was applied to the model as shown in Figure 5.20; and the resulting amplifier voltage outputs were recorded. The experiments were repeated 12 times, and the results are plotted in Figure 5.21.

Figure 5.20: Picture of stent-graft model calibrated with a series of known weights.

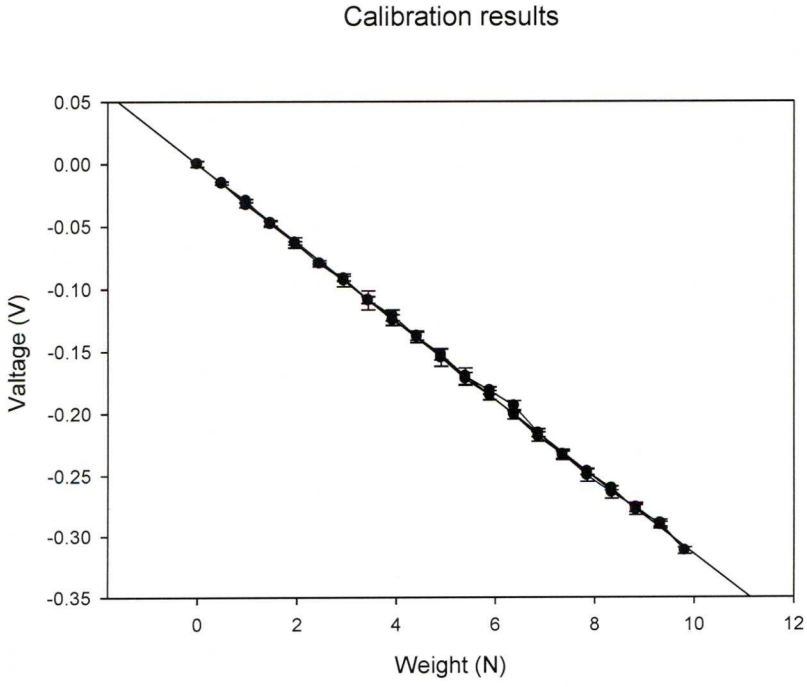

Figure 5.21: Graph showing the relationship between the applied force (in Newtons) and the output voltage (in Volts).

The results of the stent-graft model calibration suggested that this particular strain gauge could produce reliable and constant voltage, and it was suited for the LF measurements.

5.4.7 Flow circuit

After calibration, as described above, the model was placed in a pulsatile flow circuit as shown in Figure 5.22. Pulsatile flow, with waveform similar to that obtained in the abdominal aorta, was generated by a custom-built servo-controlled piston pump and a gear pump (Micropump, Vancouver, WA, USA). The circulating fluid was a 40% aqueous solution of glycerol with dynamic viscosity similar to that of blood (dynamic viscosity 3.3 x 10^{-3} Pa s and density 1098 kg m^3 at room temperature). An ultrasonic flow probe (24N, Transonic System Inc., Ithaca, NY, USA) was placed at the inlet pipe section to record the pulsatile flow. The pressure waveform just upstream of the aluminium model was also recorded using a pressure transducer (26PC, SensorTechnics UK, Rugby, UK). The pressure was set to physiological values by adjusting the resistances of the needle valves and the volume of air in the proximal and distal compliance chambers. A long inlet length of approximately 2 m was placed between the calming chamber and the stent-graft model, to ensure laminar flow developed, going into the model. The strain gauge voltage supply and instrumentation amplifier were switched on at least 2 hours prior to the experiment, to allow the strain gauges to reach thermal equilibrium. The pressure, the flow and the longitudinal force waveforms were each sampled at 100 samples/s and saved to a PC for subsequent analysis. To improve the signal to noise ratio, the data were recorded for 590 complete cycles and the average waveform was then determined.

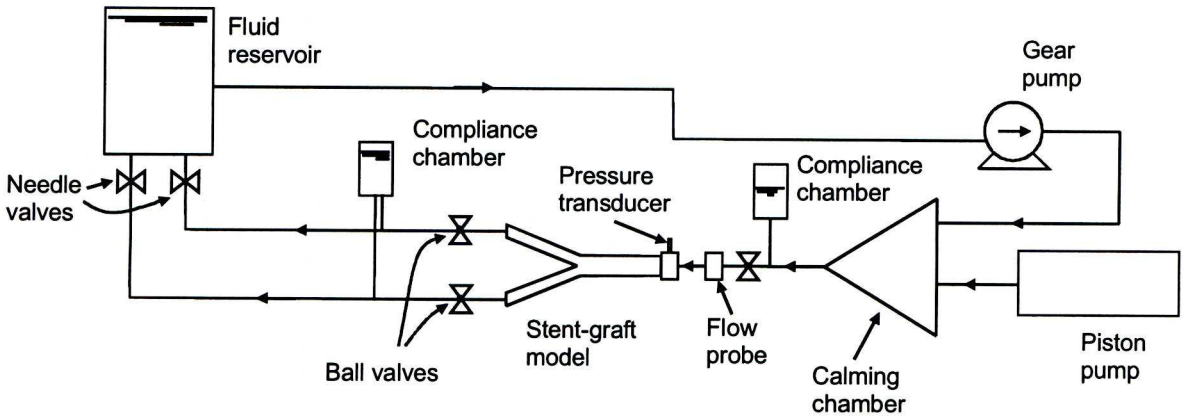

Figure 5.22 Diagram of the flow circuit.

CHAPTER 6

INVESTIGATING THE RELATIONSHIP BETWEEN THE OPTIMAL OVERSIZING AND PROXIMAL FIXATION STRENGTH IN EVAR

6.1 Introduction

The aim of endovascular treatment of aortic aneurysm is to isolate the aneurysm from the rest of the circulation, by achieving a seal between the aortic aneurysm and the stent-graft. The seal needs to be maintained against the downstream blood flow. If the stent-graft cannot withhold its position, it may move distally (migration) to cause aneurysm repressurisation and rupture.

Migration is defined as stent-graft movement in a distal direction for more than 5 mm. It is one of the commonest causes of late aneurysm rupture and reintervention (Zarins et al. 2003; Conners et al. 2003; Hobo. et al. 2006).

It is clinical practice to stent-graft oversize the aneurysm neck in order to achieve the seal. It has been suggested that appropriate oversizing can prevent stent-graft proximal Type one endoleak, by improving the proximal seal (Mohan et al. 2001).

Most of the manufacturers recommend a device oversize of 10% to 20% greater than the minor axis of the aortic neck, to achieve the optimal seal.

It is not clear whether appropriate oversizing can prevent stent-graft migration. So far, there is neither convincing data nor manufacturers' recommendations on the optimal oversizing in relation to stent-graft migration.

6.2 Aim

The aim of this study is to identify the relationship between optimal oversizing and stent-graft migration in EVAR.

6.3 Methods

The bench top experimental model consisted of freshly prepared abdominal portion of bovine aortas, proximal portion of standard Zenith stent-grafts (Cook Europe, Bjaeverskov, Denmark), a self assembled linear drive, a calibrated digital force gauge and a pressure supplying system. The oversizing was created by pressurising the aorta, in the range of human physiological blood pressure. Any change in oversizing was produced by changing the aortic pressure. The experimental model was set up by deploying the stent-graft into the pressurized aorta and then on the linear drive. By applying the force onto the stent-graft to cause it to migrate within the aorta under observation, the force could be measured with a calibrated digital force gauge. The ranges of oversizing used were 5%, 10%, 20% 30%, 40% and 50%. Further details of the methods were described in Chapter 5.

6.4 Results

The results of the pressure (mmHg), external (ED) and internal diameter (ID) relationship study are shown in Figure 6.1. This study provides the information of aortic internal diameters at the measurement points and it is

pressure related. The oversizing calculation in the next experiment will be base on the internal diameter provided from this expeirment.

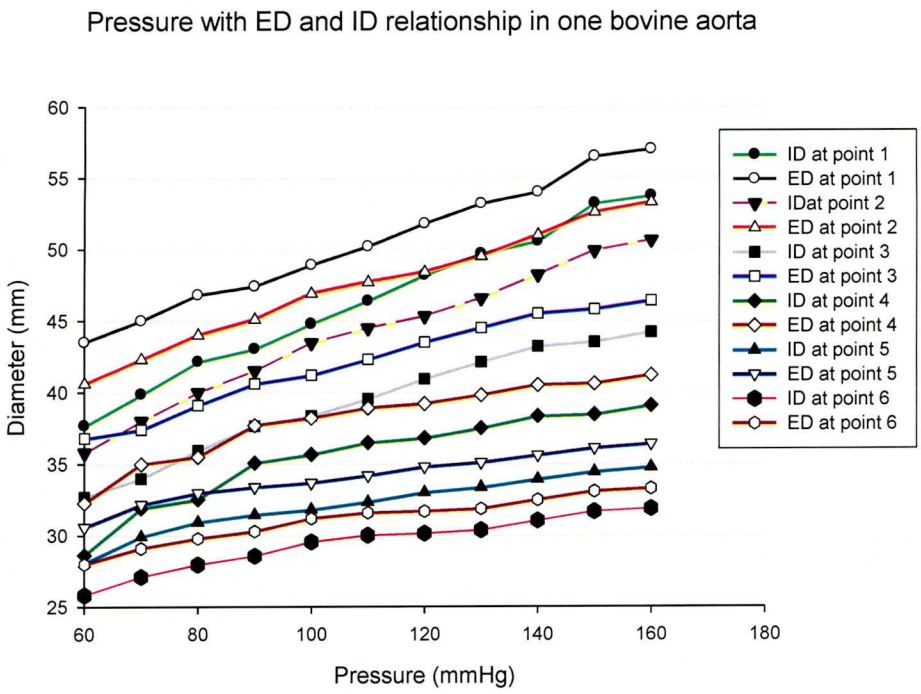

Figure 6.1: Chart of pressure v external diameter (ED); and internal diameter (ID).

In experiments using stent-grafts with barbs, the m-DF at oversizing by 5, 10, 20, 30, 40 and 50%, were 2.066±0.60N, 3.685±1.54N, 6.047±1.93N, 7.162±2.05N, 7.614±2.28N and 9.801±3.45N respectively (Table 6.1 and Figure 6.2). The m-DF showed significant difference at oversizing by 5, 10 and 20%, ($P<0.05$) and no differences at oversizing by 20, 30, 40 and 50%.

Oversize	5%	10%	20%	30%	40%	50% Oversize:
m-DF±SD(N)	2.066±0.60	3.685±1.54	6.047±1.93	7.162±2.05	7.614±2.228	9.801±3.45
P-Value	0.003	0.005	0.169	0.357	0.116	

Table 6.1: The results of m-DF±SD (N-Newton) in stent-grafts with barbs.

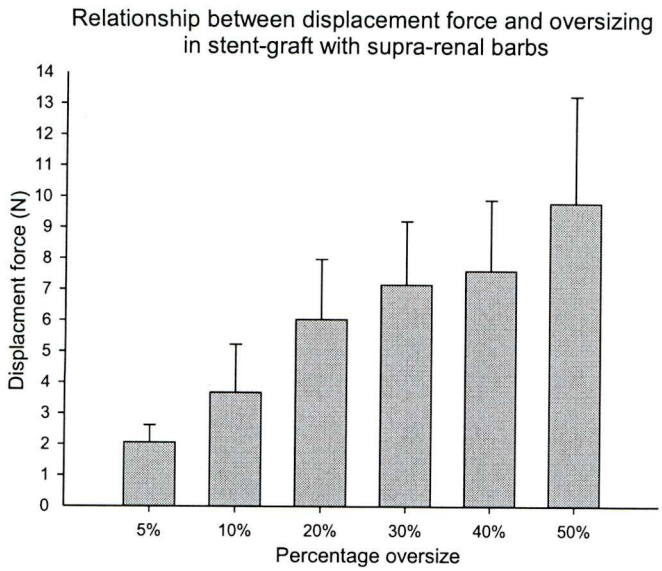

Figure 6.2: Chart of the results of the m-DF±SD in stent-grafts with barbs.

In experiments using stent-grafts without barbs, the mean DFs (m-DF) at oversizing by 5, 10, 20, 30, 40 and 50%, were 1.038±0.439 N, 2.724±1.0N, 4.238±0.80N, 4.642±0.78N, 4.837±0.78N, and 5.199±0.83N respectively (Table 6.2 and Figure 6.3). The m-DF showed significant difference at oversizing by 5, 10, 20 and 30% ($P<0.05$) and no differences at oversizing by 30, 40 and 50%.

Oversize	5%	10%	20%	30%	40%	50%
m-DF±SD(N)	1.038±0.44	2.724±1.0	4.238±0.80	4.742±0.78	4.837±0.78	5.199±0.83
P-Vaule	0.001	0.001	0.003	0.199	0.058	

Table 6.2: The results of m-DF±DS (N-Newton) in stent-grafts without barbs.

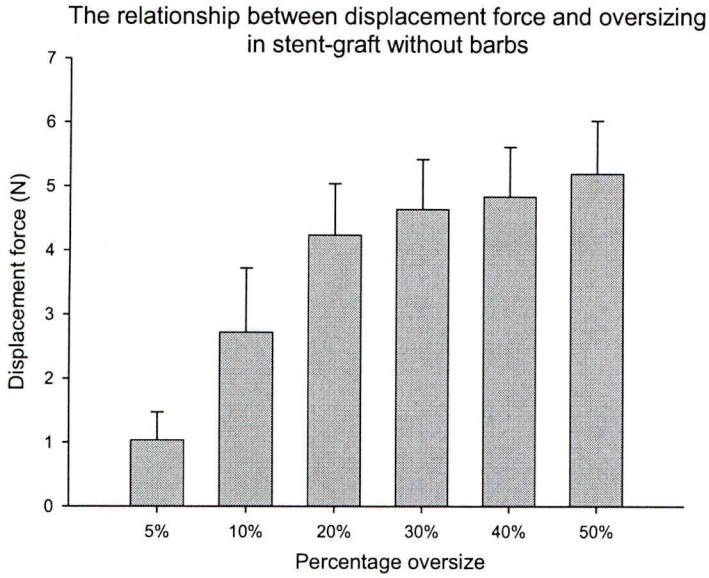

Figure 6.3: Results of the m-DF in stent-grafts without barbs.

Compare the m-DF between Zenith stent-grafts with and without barbs. The m-DF recorded was significantly higher in stent-grafts with barbs than without, at all percentage oversizing. (Table 6.3 and Figure 6.4).

Oversize	5%		10%		20%		30%		40%		50%	
With(+)/W/out(-) barbs	+	-	+	-	+	-	+	-	+	-	+	-
m-DF±SD(N)	2.066	1.037	3.685	2.724	6.047	4.239	7.162	4.642	7.614	4.837	9.801	5.2
P-Value	0.001		0.004		0.005		0.003		0.003		0.004	

Table 6.3: Comparing the m-DF in both groups

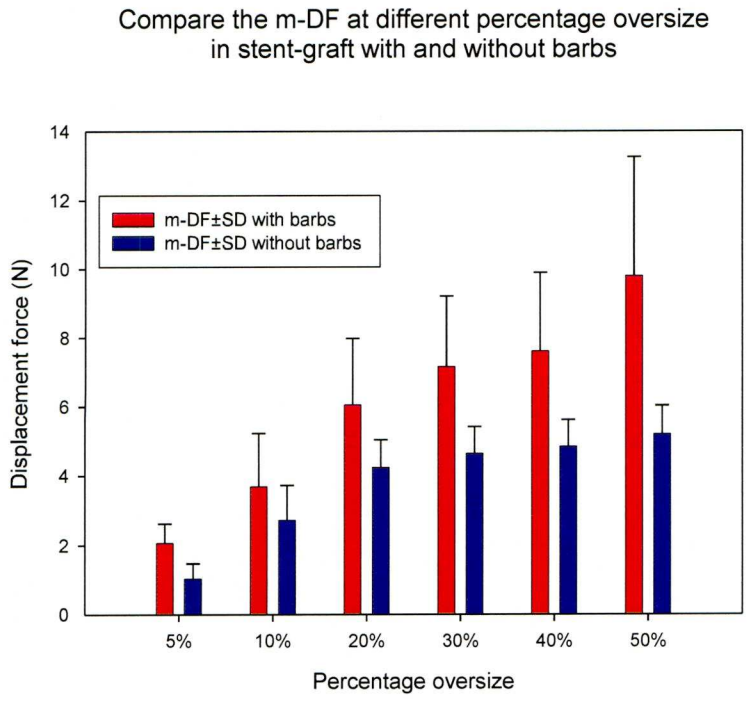

Figure 6.4: Comparing the m-DF ±SD in stent-grafts with and without barbs.

None of the experiments produced any macroscopic injury to the aortic wall after displacement (Figure 6.5). The only structural deformity noted within the stent-graft after forced displacement was upward distortion of the fixation barbs (Figure 6.6).

Figure 6.5: Picture of intima of an opened bovine aorta after experiment, showing no obvious macroscopic damage.

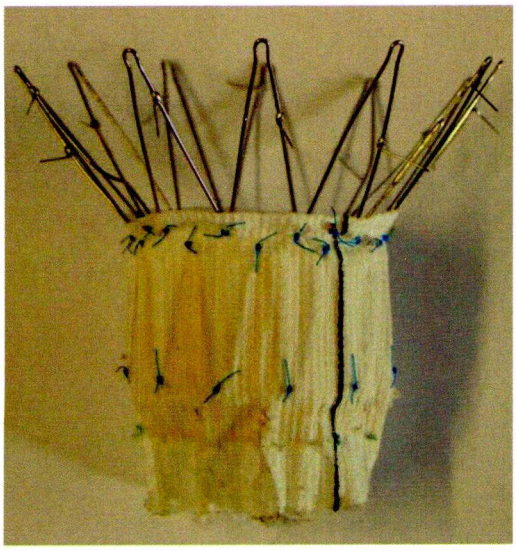

Figure 6.6: Picture showing the stent-graft after experiment, note the upward distortion of the fixation barbs.

The barbs on the bare stent were not embedded into the aortic wall at initial stent-graft deployment. Stent-graft migration occurred when the applied displacement force caused the barbs to embed in the aortic wall.

We need to point out that the total covered graft length was 17mm. This represents a suprarenal fixation device with an infrarenal neck length of 17mm.

6.5 Discussion:

Migration has occurred in all commercially available stent-grafts (van Marrewijk et al. 2005; Drury et al. 2005), and has been extensively reported in many clinical studies. The reported prevalence of migration was from under 3% to 28% (Tonnessen et al. 2005; Zarins et al. 2003; van Herwaarden et al. 2007). The factors affecting migration were type of stent-grafts used, aortic aneurysm morphological characteristics and the length of study follow-up time (Tonnessen et al. 2005; Zarins et al. 2003; van Herwaarden et al. 2007). The proximal aortic neck length, diameter and angle seem to have great influence on the risk of proximal

stent-graft migration after EVAR. (Tonnessen et al. 2005; Zarins et al. 2003, Fulton et al. 2006; Albertini et al. 2000; Leurs et al. 2005). The other risk factors that have also been studied are maximum aneurysm diameter, stent-graft configuration (aortic tubes, aortomonoiliac, bifurcation grafts), the type of proximal stent-graft fixation (suprarenal / infrarenal, with / without hooks and barbs) and the extent of stent-graft oversizing (Sternbergh III et al. 2004; Waasdorp et al. 2005; Mohan et al 2002; Leurs et al.2005; Faries et al. 2002; Resch et al. 2000).

Clinical studies into the relationship between proximal oversizing and graft migration have produced conflicting results. Some studies suggest there is no significant association between oversizing and migration (Sampaio et al. 2005; Cao et al. 2002).

In some large multicentre studies with implantation of the Zenith, AneuRx and different types of stent graft studies (Zarins et al. 2003; Sternbergh III et al. 2004; Mohan et al. 2002), only Sternbergh et al found a significant association. >30% oversizing significantly increased the risk of migration compared with ≤30% oversizing (14% v 1%, odds ratio 18.4; p=0.002) (Sternbergh III et al. 2004).

Mohan et al. investigated the EUROSTAR multicentre database (N = 2,862) and found 99 patients with migration (3.5%). Univariate analysis revealed no association between oversizing and graft migration, and the migration incidence did not differ significantly between several types of stent-graft (Mohan et al. 2002).

There are experimental studies investigating the relationship between oversizing and the required force for stent-graft displacement. Malina et al. used cadaveric aortas to measure the longitudinal distraction that was required to dislodge Zenith-stents from the aorta (Malina et al.1998).

This study suggested that the stent-graft oversizing had no effect or only slightly increased the required force for displacement of stent-grafts with or without barbs, respectively.

Lambert et al. investigated the longitudinal load needed for 5 mm dislodgement of 24 mm nitinol self-expandable stent-grafts in cadaveric aortas. Wider aortas with relatively less oversized stent-grafts needed less load to dislodge the stent-grafts compared with smaller aortas with relatively more oversizing, respectively (Lambert et al.1999). A second experiment measured an increased radial depression of the stent with an increasing applied radial load. More deformation of the graft generates a greater radial force, which therefore is a benefit of oversizing (Lambert et al. 1999).

Our study investigated the longitudinal force needed for 5 mm displacement of Zenith stent-grafts in bovine aortas with a relatively short neck (17 mm). A much wider range of oversizing was used in our study (5, 10, 20, 30, 40 and 50%). The results suggest that in stent-grafts with barbs, the m-DF showed significant difference at oversizing by 5, 10 and 20% and no difference at oversizing by 20,

30, 40 and 50%. In stent-grafts without barbs, the m-DF showed significant difference at oversizing by 5, 10, 20 and 30% and no difference at oversizing by 30, 40 and 50%.

Comparing the m-DF between stent-grafts with and without barbs, the m-DF recorded was significantly higher in stent-grafts with barbs than without, at all percentage oversizing.

These findings suggest that oversizing has significant effects on stent-graft migration. In stent-grafts with barbs, optimal oversizing of 20% is needed to produce a beneficial effect against stent-graft migration, and 30% in stent-grafts without barbs. The barbs increase the overall proximal fixation strength against migration.

Another important observation from this study was none of the experiments produced any macroscopic injury to the aortic wall after displacement. This was due to the barbs from the bare stent not actually embedding into the aortic wall after deployment. Further study is needed to explore further into this phenomenon.

Since our experiment was a bench top laboratory experiment, some of the necessary in-vivo parameters were not reproduced. This has led to numerous limitations in the study. The aortas used were straight, healthy bovine aortas,

therefore the other factors such as aortic neck angulations, thrombosis, calcifications, associated with stent-graft migration in the group of elderly human population with diseased aortas were not considered. We recorded the DF in one-off migration of the stent-graft. In vivo however, migration is the result of repetitive forces exerted on the stent-graft over a considerable length of time by pulsatile blood flow (Resch et al. 2000; Malina et al. 1998). Clinical study has suggested that the iliac fixation also has a significant impact on proximal stent-graft migration during EVAR follow-up (Waasdorp 2009). Since we truncated the stent-graft to the proximal portion only, the effect of iliac fixation was not considered. As the different stent-grafts may have different designed fixation strength, the "fact value" of the m-DF cannot represent any other stent-graft device. Though oversizing was accurately produced, it was not true stent-graft oversizing; the oversizing was "created" by changing the aortic diameter.

6.6 Summary

In summary, optimal proximal oversizing has a significant effect on proximal fixation strength, and therefore on stent-graft migration. To produce the maximal proximal fixation strength, the optimal oversizing required for stent-grafts with barbs is 20%, and for stent-graft without barbs, is 30%. Barbs increase the overall proximal fixation strength.

CHAPTER 7

COMPARISON OF THE FIXATION STRENGTH OF STANDARD AND FENESTRATED STENT-GRAFT FOR EVAR

7.1 Introduction

Since endovascular abdominal aortic aneurysm (AAA) repair (EVAR) was introduced more than a decade ago, the technique has been widely accepted, worldwide. Clinical trials have demonstrated short-term survival benefit over open repair of large AAAs (Greenhalgh et al. 2004; Prinssen et al. 2004). Although stent-graft design and EVAR techniques have much improved, the durability of stent-grafts still raises concerns. One of the most important complications affecting the long-term success is stent-graft migration; that is, movement of a fully deployed stent-graft relative to the vascular anatomy, which has the potential to cause attachment-site endoleak and even aneurysm rupture (Greenhalgh et al. 2004; Prinssen et al. 2004; Alimi et al, 1998; Torsello et al.1998; Lumsden et al,1995). Deployed stent-grafts constantly face physiological forces (Liffman et al.2001, Mohan et al, 2004, Morris et al, 2002) that can initiate migration, and these devices should be designed to resist such displacement.

Fenestrated stent-grafts have been introduced to extend the applicability of EVAR to patients with an aneurysm neck that is too short to satisfactorily position a conventional stent-graft (Politz et al 2000; Zarins et al 2000). A fenestrated stent-graft has fabric that extends to a level above one or more visceral arteries. Perfusion of the visceral arteries below the fabric margin is preserved via one or more fenestrations in the stent-graft fabric that are incorporated during

manufacture and positioned accurately at the time of deployment. Usually stents are placed through the fenestration into the visceral arteries to provide additional anchorage to the stent-graft, although they are not intended primarily for this purpose.

7.2 Aim

The aim of this study was to compare the proximal fixation strength of standard and fenestrated stent-grafts in an in vitro bovine aortic model.

7.3 Methods

The bench top experimental model consisted of freshly prepared abdominal portion of bovine aortas with branches, proximal portion of a standard Zenith stent-graft (Cook Europe, Bjaeverskov, Denmark), or self-constructed fenestrated stent-graft, self assembled linear drive, a calibrated digital force gauge and a pressure supplying system. The oversizing was created by pressurising the aorta in the range of human physiological pressure. Any changes in oversizing were produced by changing the aortic pressure. The experimental model was set up by deploying the standard and fenestrated stent-graft into the pressurized aorta; the fenestration was created by deploying a 6mm AVE stent into the suited branch. The aorta and stent-graft assembly was then placed on the linear drive. By applying the force onto the standard and fenestrated stent-grafts to cause them to migrate within the aorta under observation, the force could be measured, with a calibrated digital force gauge. Fenestrated stent-grafts were constructed with a single 6 mm-wide

fenestration at a distance of 21 mm from the fabric edge (Figure. 6.6 B). The fenestrations were not reinforced. The oversizing used was 5%, 10% and 20%. Further details of the method are described in Chapter 5.

7.4 Results

Figure 7.1 shows the results of an aortic intraluminal pressure and aortic internal diameter relationship study.

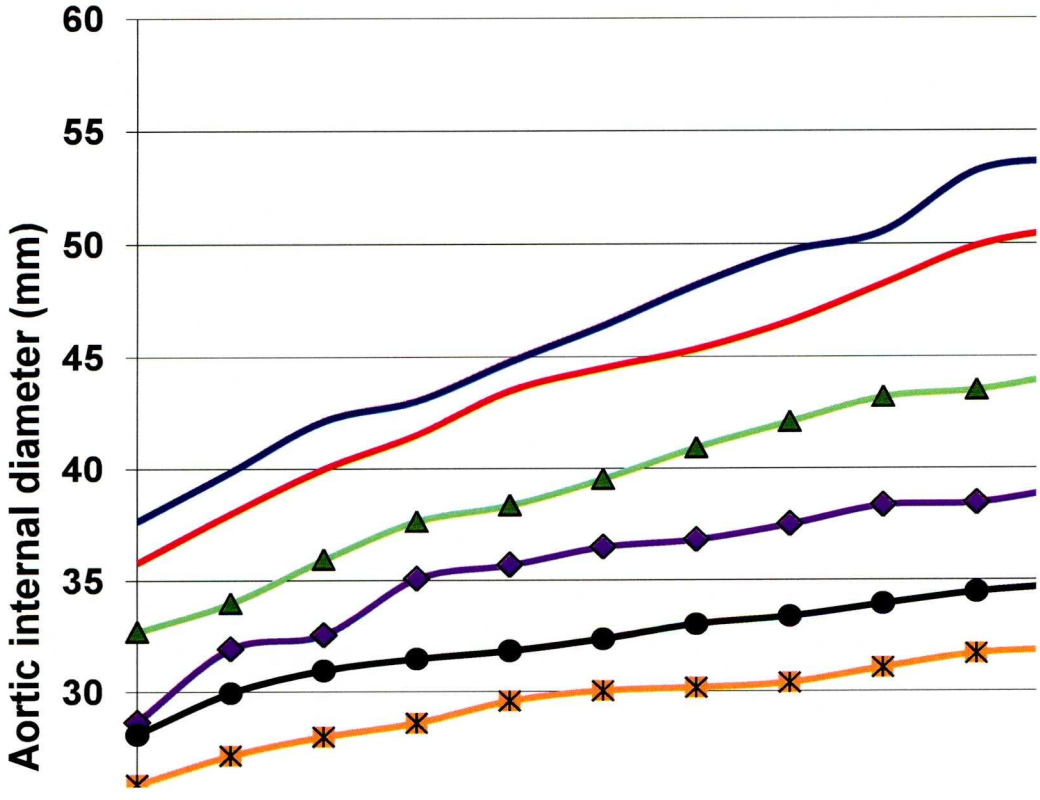

Figure 7.1: Chart shows how the aortic internal diameter increases with intraluminal pressure.

With gradually increasing distraction force, the stent-graft migration was noted to occur in 2 distinct phases. There was an initial yield, corresponding to a displacement up to about 5 mm, which was attributed to embedding of the barbs

into the aortic wall. Once this phase was complete, the stent-graft was able to resist migration for a period until a second yield occurred with increasing force, followed by movement of the stent-graft in relation to the aorta. The peak displacement forces (Table 7.1) corresponding to the 2 phases were described as initial displacement force (IDF) and final displacement force (FDF), respectively. For standard stent-grafts, the mean values of both IDF and FDF at 20% oversizing were significantly greater than the corresponding values at 10% oversizing ($p<0.001$), which in turn were greater than those at 5% oversizing ($p = 0.02$). Results with fenestrated stent-grafts show a similar trend with the exception of a lack of significant difference between 20% and 10% oversizing levels ($p = 0.054$). Both the initial and final displacement forces were significantly higher with fenestrated stent-grafts than with standard stent-grafts ($p<0.001$) at any degree of oversizing.

	5% Oversizing		10% Oversizing		20% Oversizing	
	IDF	FDF	IDF	FDF	IDF	FDF
Standard	3.39±0.37	8.10±0.92	4.32±0.63	10.76±1.74	7.69±1.18	16.82±0.92
Fenestrated	10.48±1.23	22.56±1.60	11.45±1.48	28.24±1.56	12.12±1.42	33.01±1.75

* $p<0.001$ for standard vs. fenestrated at each oversizing level.

TABLE 7.1: Comparison of Initial Displacement Force (IDF) and Final Displacement Force (FDF) for 3 Oversizing Levels in Standard and Fenestrated Stent-Grafts.

The mean initial and final displacement forces in standard and fenestrated stent-grafts for oversizing of 5%, 10%, and 20% are shown graphically in Figure 7.2

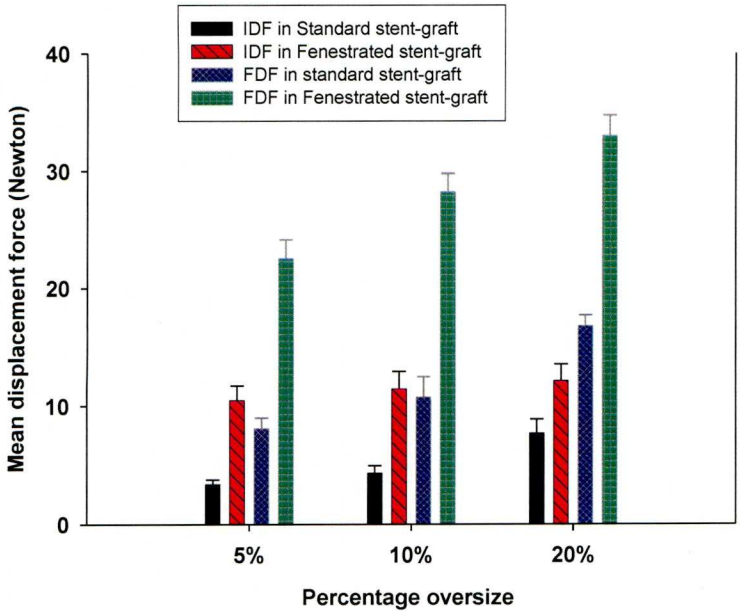

Figure 7.2: Graph showing the mean initial and final displacement forces in standard and fenestrated stent-grafts for oversizing of 5%, 10%, and 20%.

None of the experiments produced any macroscopic injury to the aortic wall after displacement (Figure 7.3A). The only structural deformity noted within the stent-graft after forced displacement was upward distortion of the fixation barbs (Figure 7.3B). The AVE stents appeared compressed and bent after the experiments (Figure 7.3C).

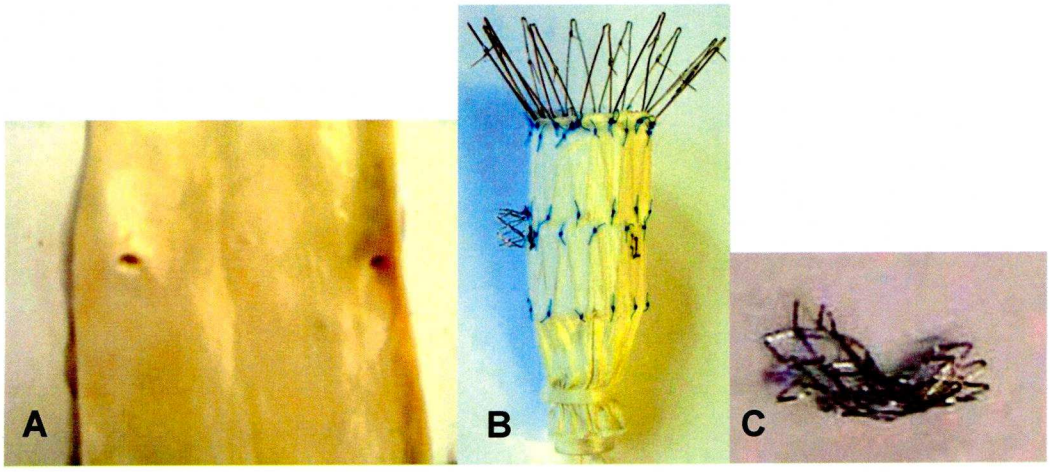

Figure 7.3: There is no macroscopic injury to the aortic wall after displacement experiment (A). The only structural deformity noted within the stent-graft after forced displacement was upward distortion of the fixation barbs (B). Appearance of the AVE stent after final displacement of the stent-graft (C).

During the experiments, we also observed that stent-graft migration was not in a straight line with the direction of force applied. When migration occurred, the opposite fenestration stent side of the stent-graft migrated first.

7.5 Discussion

Traditional stent-graft designs rely upon physical attributes of a deployed stent-graft, such as columnar strength and radial force, to maintain a durable fixation. Fixation appendages, such as hooks or barbs incorporated at attachment sites, and aortic neck length also increase fixation strength (Lambert et al, 1999; Veerapen et al. 2003; Resch et al, 2000, Malina et al. 1998). The main factors predisposing to late migration are late dilatation of the aneurysm neck, haemodynamic forces acting upon the stent-grafts, and mechanical disintegration of the device. Poor quality of the vessel at the proximal fixation zone and underutilization of the infrarenal neck at the time of graft deployment also reduce the fixation strength and predispose to migration (Wolf et al. 2001; Sternbergh et al

2002; Matsumura et al. 2000, Franko et al. 1998). Fenestrated stent-grafts were introduced primarily to preserve renal or mesenteric branch vessel perfusion while recruiting the aortic wall at the level of these branches, to provide proximal seal and fixation (Anderson et al, 1999; Browne et al 2001). Stents are routinely placed from the aortic lumen into the visceral arteries through the fenestrations, to enhance the fixation strength of the stent-graft (Verhoeven et al. 2004). However, migration of a fenestrated stent-graft could result in distortion of the visceral artery stent and consequent loss of patency of this vessel, in addition to the other consequences of migration. Although fixation strengths of standard stent-grafts have been reported (Lambert et al. 1999; Veerapen et al. 2003; Resch et al. 2000, Malina et al. 1998), there have been no reports relating to fenestrated stent-grafts. Furthermore, previous reports of fixation strength were based on experiments conducted on nonpressurized aortas, an important limitation to understanding the relationship between oversizing and fixation strength. As the experiments reported here were conducted with pressurized aortas, the results are likely to better represent the clinical situation.

An important observation of this study was the mode of migration of a stent-graft designed with fixation barbs. In the initial phase, a few millimetres of caudal migration, usually not exceeding the length of the barb (5 mm), occurred at a lower force as the barbs embedded into the aortic wall. More substantial force was required to cause subsequent migration in the second phase. The initial phase of migration is in accord with anecdotes from physicians familiar with similar stent-graft systems; they report that the stent-grafts may "settle" a few millimetres downwards after deployment. It is recognized that the Zenith stent-graft has a low

incidence of migration, but we are unable to compare the fixation strength of different devices in our study, since only one make of stent-graft was used (van Marrewijk et al. 2005).

When comparing the initial displacement force (for stent-graft migration by 5 mm) with the results of stent-graft with barbs from Chapter 6 in standard stent-grafts, the value was generally higher at the same percentage of oversizing. In Chapter 6, in experiments using stent-grafts with barbs, the m-DF at oversizing by 5% was 2.066±0.60N, 10% was 3.685±1.54N, 20% was 6.047±1.93N, the results of the initial displacement force at oversizing by 5% was 3.39±0.37N, 10% was 4.32±0.63N, 20% was 7.69±1.18N. The settings of these two experiments were the same apart from the seal zone length in this experiment was 36mm, and 17mm in Chapter 6. Clearly, the longer seal zone length here produced a higher initial displacement force.

The final displacement forces in standard stent-grafts varied from 8.1 to 16.8 N, depending on the percentage oversizing. These values are smaller than those reported by Veerapen et al (Veerapen et al. 2003) and Resch et al (Resch et al. 2000). Although the former authors reported experiments with oversizing of 10% to 20%, Resch and colleagues did not provide this information.

The main difference with the present study is that the oversizing was accurately determined via known pressure-diameter relationships of the bovine aorta. It

should be pointed out that the pressure per se did not have an influence on the displacement forces. The graft material was and remained porous to the saline during the experiments, and the pressure in the graft lumen was therefore similar to that in the aorta. Consequently, there was no net force acting on the graft due to the applied pressure.

The discovery of biphasic movement of this type of stent-graft upon application of a dislodging force raises some important issues. Full recruitment of the barbs into providing fixation strength appears to involve caudal movement of the stent-graft by a few millimetres, as the barbs embed into the aortic wall. No such movement is caused deliberately in standard clinical practice. Should it occur naturally after deployment, the movement of a stent-graft by a few millimetres seldom causes significant problems with standard stent-grafts. It may, however, have significant implications for fenestrated stent-grafts. Since the barbs may not be fully engaged at the position of initial deployment, there is a risk of transferring some of the haemodynamic migratory forces to the interface between the stent-graft and the side-branch stent, immediately after completion of aneurysm repair. Small-diameter stents that are suitable for side-branch placement are not designed to withstand the resultant asymmetric hoop stress. Failure or significant distortion of side-branch stents due to such stress can lead to loss of side-branch patency. A mechanism by which the initial phase of migration could be eliminated or made to occur in a controlled manner would have the potential to eliminate adverse effects. Moulding of the fixation areas using a conformable balloon may cause embedding of the barbs and eliminate the initial phase of migration or stent-graft settling.

Another important finding of this study was a relationship between oversizing and fixation strength; fixation strength increased with increasing oversizing up to 20%, which supports routine oversizing with self-expanding stent-grafts. In the case of fenestrated stent-grafts, however, the fixation strength did not increase significantly above 10% oversizing. This may be due to the fact that most of the fixation strength here was provided by the side-branch stent acting as an anchor, rather than by the interaction between the stent-graft and the aortic wall.

Although the methods of this study represent an enhancement compared with earlier in vitro studies of fixation strength (Lambert et al, 1999; Veerapen et al. 2003; Resch et al. 2000, Malina et al. 1998), there are a number of limitations to this study. The aortas used were straight tubular segments from healthy animals, and as such could not replicate some of the features of aneurysm anatomy, such as neck angulations, conical shape, or presence of calcification, or thrombus. The applied distraction force was incremented gradually and thus may be functionally different from the repetitive forces that stent-grafts are subjected to in vivo (Zarins et al, 2005). Because of the natural taper of the aorta, the vessel was reversed in the experiment so that the stent-graft was made to migrate from the narrow to the wide segment, thereby potentially underestimating the fixation strength. Any error is likely to be small, but we considered that the alternative orientation was a worse option since this may potentially result in falsely high fixation strengths.

Although the length of the stent-graft used was 53 mm in both groups, only 36 mm of the covered section of the stent-graft was actually in contact with the aortic wall. This is at the upper end of the range of graft overlap with the aortic neck in vivo.

The experiments were designed to measure the displacement force of the isolated proximal portion of the stent-graft, so truncated devices were used. We realize that the use of a complete bifurcated device may influence the measured forces, but the model used did not allow the effect to be investigated.

7.6 Summary

These experiments demonstrate that proximal fixation strength of a self-expanding stent-graft with a proximal bare stent and barbs, increases, with increasing degree of oversizing up to 20%, and that a fenestrated stent-graft configuration confers a greater proximal fixation than conventional devices. With such stent-graft design, full engagement of fixation barbs may cause movement of the stent-graft by a few millimetres before the full fixation strength of the device comes into action. This observation may have significant implications for fenestrated stent-graft design.

CHAPTER 8

INVESTIGATION OF THE OPTIMAL OVERSIZING REQUIRED FOR AN EFFECTIVE SEAL IN STANDARD AND FENESTRATED EVAR

8.1 Introduction

The aim of endovascular treatment of aortic aneurysm is to isolate the aneurysm from the rest of the circulation; hence obtaining an effective seal between the endoluminal stent-graft and the aorta, above and below the aneurysm. Failure to achieve seal will lead to endoleak and eventually aneurysm rupture.

Endoleak is defined as persistent blood flow outside the lumen of the Endoluminal graft but within the aneurysm sac, as determined by an imaging study (White et al 1996; White et al 1997).

There are four types of endoleak according to the origin and site. Type I endoleak is defined as the persistence of a perigraft channel of blood flow caused by inadequate or ineffective seal at either the proximal (proximal Type I endoleak) or distal (distal Type I endoleak) attachment zones (Chaikof et al 2002).

Proximal Type I endoleak may result in serious consequences if it remains untreated. Data from the EUROSTAR registry has suggested that proximal Type I endoleak has much higher risks of late conversion (Harris et al 2000; Vallabhaneni et al 2001) and rupture (Marrewijk et al 2002). Also, compared with distal Type I endoleak, the proximal Type I endoleak has a significantly higher risk of aneurysm rupture (Mohan et al 2001).

In clinical practice, oversizing of aortic stent-grafts is an essential step to prevent Proximal Type I endoleak. However, there is no consensus regarding the optimal degree of oversizing needed, in particular, in relation to the aortic neck length.

8.2 Aim

This study is designed to investigate the optimal degree of oversizing required for an effective seal in standard and fenestrated EVAR.

8.3 Methods

The in-vitro model consisted of a sealed, truncated Zenith stent-graft (Cook Europe, Bjaeverskov, Denmark) which was deployed into the pre-determined measurement point of the bovine aortic section. In a fenestrated stent-graft, a 6 mm AVE stent was used to insert through the fenestration, into the side branch of bovine aorta. A purpose built system generated pulsatile flow, mimicking infrarenal aortic flow. It consisted of a piston pump (self assembled) to provide pulsatile flow, and a gear pump (HG 0024 Micro pump INC, Vancouver, WA, USA), to provide steady flow. 40% glycerol solution with physiological viscosity was used as circulating fluid. A pressure sensor and an ultrasonic flow meter (Transonic HT107/HT207 Medical Flowmeter, Ithaca, NY 14850 USA) measured pressure and flow continuously during the experiment. The system was connected to a computer for controlling and monitoring the pressure and flow (Figure 5.8 & 5.9). Details of the methods are described in Chapter 5.

8.4 Results

With gradually increasing pulsatile pressure, leaks occurred in an intermittent fashion. Leaks were observed in the systolic pressure phase and stopped in the diastolic phase.

The results of all three tests in standard stent-graft are shown in figure 8.1. With increasing seal zone length, the degree of "optimal oversize" required for a seal is reduced. The "optimal oversize" at "aortic seal zone lengths" of 10 mm, 15 mm, 20 mm, 30 mm and 40 mm was 20.44%, 16.42%, 10.25%, 7.09%, 4.22% in test run 1, 20.87%, 16.70%, 10.66%, 7.35%, 4.88% in test run 2 and 23.11%, 18.33%, 11.71%, 8.62%, 5.45% in test run 3.

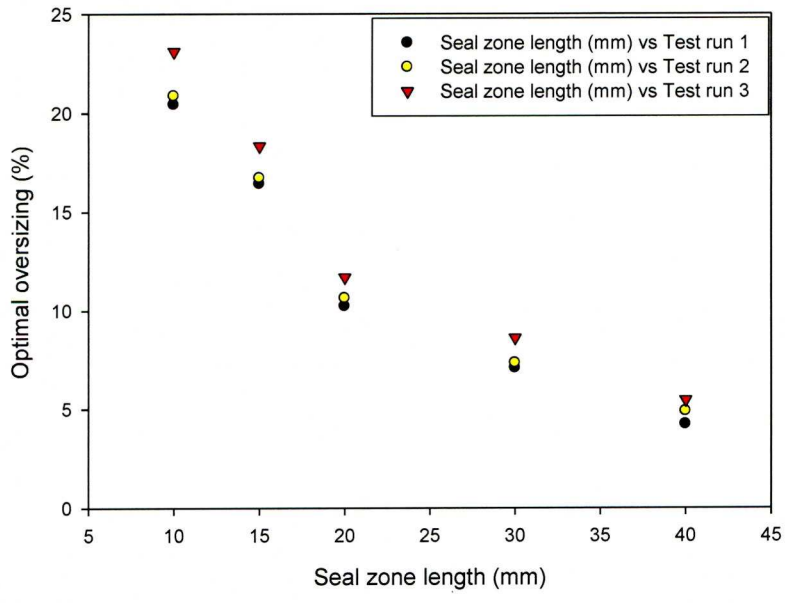

Figure 8.1: Chart of results of the "optimal oversize" in standard stent-graft.

The results of experiments on fenestrated stent-graft are shown in figure 8.2. Similarly, with increasing seal zone length, the degree of "optimal oversize" required for a seal is reduced. The "optimal oversize" at "aortic seal zone lengths"

of 5 mm 10 mm 15 mm and 20 mm was 19.12%, 14.72%, 9.41%, 5.61% in test run 1, 20.71%, 15.87%, 10.44%, 6.11% in test run 2 and 20.43%, 15.42%, 10.89%, 6.04% in test run 3. However, when the seal zone length was reduced to 0 mm, endoleak was observed in the full range of oversizing.

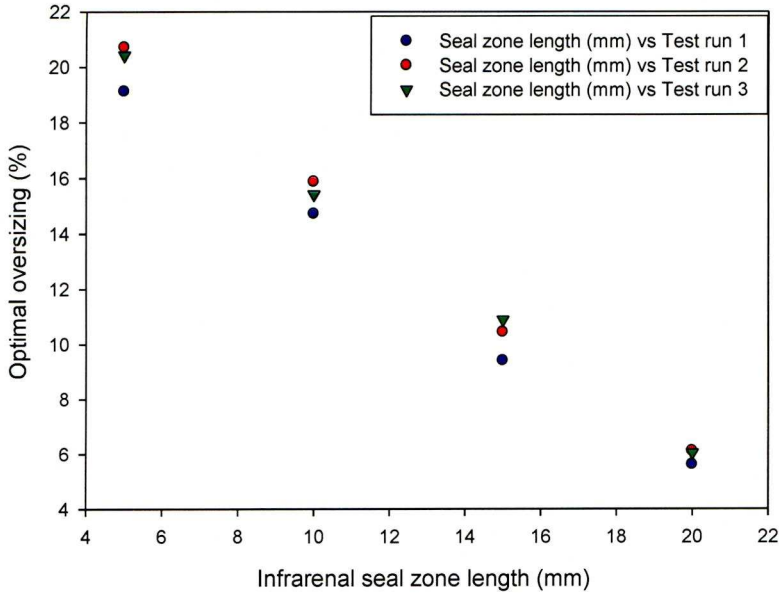

Figure 8.2: Chart of results of the "optimal oversize" in fenestrated stent-graft, the total seal zone length will include the suprarenal length of 21mm.

The results of experiments with a rigid sleeve over the aorta, to eliminate oversize variation, showed that no leak was observed in the pulsatile pressure range from minimum diastolic pressure of 60 mmHg to the maximum systolic pressure of 235 mmHg.

8.5 Discussion

Proximal Type I endoleak is the most important cause of abdominal aortic aneurysm (AAA) rupture after EVAR (Schlosser J et al 2009). It is also the most common reason for re-interventions (Hobo et al 2006).

A three year study in regard to proximal Type I endoleak has suggested an incidence of 4% (Sampaio et al 2004) and perioperative incidence from the Eurostar registry was 3.3% (Mohan et al 2001).

Clinical studies suggest that the appropriate oversizing of stent-graft to aortic neck can prevent proximal Type I endoleak and stent-graft migration. With effective oversizing, a secured fixation and seal can be achieved. However, it is not clear what the most appropriate oversizing is to achieve the optimal seal. Clearly, under oversizing (or undersizing) of a stent-graft will result in incomplete and inadequate apposition of the stent-graft to the aortic wall with subsequent proximal Type I endoleak or inadequate fixation with the potential risk of migration. On the other hand, excessive oversizing may increase the risk of complications, such as stent-graft infolding or dilatation of the aneurysm neck, with subsequent migration and endoleak of the stent-graft (Schurink et al 1999; Conners et al 2002; Sternbergh et al 2004).

The currently published studies have suggested the mechanisms by which stent-graft oversizing may induce, or prevent, proximal Type I endoleak. Excessive oversizing may cause stent-graft folding with subsequent risk of proximal Type I endoleak. Under oversizing (or undersizing) will result in an inadequate seal, leading to proximal Type I endoleak (Matsumura et al 1998; Petrik et al 2001; Dias et al 2001; Sampaio et al 2004).

In clinical practice, it has been recommended that to achieve an effective proximal seal, the stent-graft oversizing should be 10%-20% in self expanding stent-grafts (Mohan et al 2001; Greenberg et al 2004). However, there is currently no consensus with regard to the stent-graft optimal oversizing for EVAR. Neither is it known whether the same degree of oversize is needed for different aortic neck lengths.

The aim of stent-graft oversizing is to obtain an effective seal. It is not necessary and can be risky to excessively oversize the aortic neck beyond the minimal degree of oversizing required (defined as optimal oversizing in our study). So our study is to identify the optimal degree of oversizing for effective seal and minimise the risk of adverse effects of excessive oversizing.

Our study suggests that the optimal oversize for effective seal varies, dependent on the length of aortic neck. In general, greater oversizing is required for shorter aortic neck length in both standard and fenestrated EVAR. In experiments with standard stent-graft, at aortic neck length of 40 mm, only 4% oversizing is needed to achieve an effective seal. When aneurysm neck length is as short as 10 mm however, 20% oversize is needed to achieve effective seal. In experiments with fenestrated (with bare stent) stent-graft, at aortic neck length of 20 mm, only 6% oversize is needed to achieve the seal. When aneurysm neck length is as short as 5 mm, 20% oversize is needed to achieve effective seal.

In combining the results from fixation studies in chapter 6 and 7, the practical recommendations for clinical practice would be 10% to 20% oversize for relatively short seal zone length (17-20 mm) to achieve the best results both for seal and

fixation. Whereas for relatively longer seal zone length (36-40 mm), the oversize can be ranged from 4% to 20%.

In our experiment, every effort was made to simulate the in-vivo situation. Pulsatile flow mimicked the infrarenal aortic flow. However, some of the other in-vivo parameters are more difficult and even impossible to reproduce, in a bench top model. This has led to numerous limitations in this study. The aortas used were straight tubular segments from healthy animals and as such cannot replicate the features of aneurysm anatomy such as neck angulations, conical shape, and presence of calcification or thrombus. There was no "aneurysm sac" therefore the effect of aneurysm diameter and the pressure gradients were not considered. Though a pulsatile pressure system was used, the purpose was to generate variations in oversize. The pressure range was beyond the normal human blood pressure range. However, these factors are unlikely to overwhelmingly limit the value of the conclusions that can be drawn from these findings.

8.6 Summary

In summary, the optimal oversize for appropriate seal is dependent on the aortic neck length in both standard and fenestrated EVAR. In general, the optimal oversizing is inversely related to seal zone length. We suggest that with shorter seal zone length more oversize is required for an appropriate proximal seal. For fenestrated EVAR with bare stent, a seal can be achieved at infrarenal neck length as short as 5 mm.

CHAPTER 9

MEASUREMENT OF PULSATILE HAEMODYNAMIC FORCES IN A MODEL OF A BIFURCATED STENT GRAFT FOR ABDOMINAL AORTIC ANEURYSM REPAIR

9.1 Introduction

The success of EVAR depends on secure fixation of the sent-graft in the patient's aorta. The degree of fixation should be such that the device is able to withstand the downward haemodynamic forces due to pulsatile pressure and flow. The fixation strength of stent-grafts has been estimated by measuring the longitudinal displacement force at the proximal fixation site of various commercially available stent-grafts in a cadaveric model (Resch et al, 1999; Veerapen et al, 2003). The average fixation strength ranged from 4.5 N to 25 N, compared to 150 N for the hand sewn anastomosis of conventional repair.

Mathematical models have been developed previously to derive theoretical estimates of the haemodynamic forces that may be exerted on stent-grafts *in vivo*. (Liffman et al. 2001, Mohan et al, 2002, Morris et al. 2004). Mohan et al showed that hypertension, aneurysm geometry and iliac angulation, amongst other factors, were significantly associated with stent-graft migration, and consequent loss of fixation (Mohan et al, 2002). These findings were validated using a simple one-dimentional analytical model based on momentum equation, not accounting for the pulsatility of blood flow and the viscosity of the fluid. It was shown that under certain conditions, the longitudinal force (LF) on a stent-graft due to blood flow and pressure may exceed the fixation force, thus causing stent-graft migration.

9.2 Aim

The purpose of this study was to develop an experimental method to measure LF in a model of a stent-graft under pulsatile flow of a viscous fluid. A number of test runs were carried out to assess the feasibility of the technique and compare the experimental data with the analytical predictions.

9.3 Theoretical Model

Mohan et al (2002) considered a simple model of an idealized bifurcated device shown in Figure 8.1 to estimate the longitudinal force f_x exerted on the EVAR device. It is assumed that the bifurcation is planar and symmetrical, and the blood flow is distributed equally through two iliac limbs of equal diameter (this is a simplification of the situation in vivo where the stent-graft has to conform to irregular three-dimensional geometry of the AAA). In addition the flow is assumed to be steady and the fluid is assumed to be inviscid, i.e. the viscosity is zero.

The change in direction and velocity of flow due to the diameter change and the bifurcation angle causes a change in the momentum of the fluid. The momentum change and the pressure forces acting at the inlet and outlets result in a net longitudinal force f_x on the device which must be opposed to prevent its distal migration. Mohan et al (2002) derived the following expression (Equation 9.1) for f_x.

$$P_1 A_1 - 2P_2 A_2 \cos\theta - f_x = \rho Q\left(\frac{U_2}{2}\cos\theta + \frac{U_2}{2}\cos\theta - U_1\right) \qquad (9.1)$$

Where P_1, A_1, U_1 and P_2, A_2, U_2 are the pressure, cross-sectional area and velocity at the inlet and outlet, respectively; p is the density of the fluid and Q is the volume flow rate. The first two terms on the left hand side of equation 9.1 represent the pressure forces at the inlet and outlets acting on areas A_1 and A_2, respectively. f_x is the axial component of the force exerted by the bifurcation on the fluid. The right hand side of equation 9.1 represents the rate of increase of axial component of momentum.

Using Bernoulli's and continuity equations, the pressure P_2 and velocity U_2 at the outlet can be expressed in terms of U_1, P_1 and A_1 and the equation for f_x can be re-written as follows:

$$f_x = P_1 A_1 + \rho A_1 U_1^2 - \rho \frac{A_1^2}{2A_2} U_1^2 \cos\theta - 2A_2 \cos\theta \left[P_1 + \rho \frac{U_1^2}{2} \left(1 - \frac{A_1^2}{4A_2^2} \right) \right] \qquad (9.2)$$

f_x can be readily calculated for a given device geometry and haemodynamic conditions using equation 9.2. In the transverse direction, the pressure and momentum forces cancel out because of the symmetry and equal flow distribution and therefore $f_y = 0$.

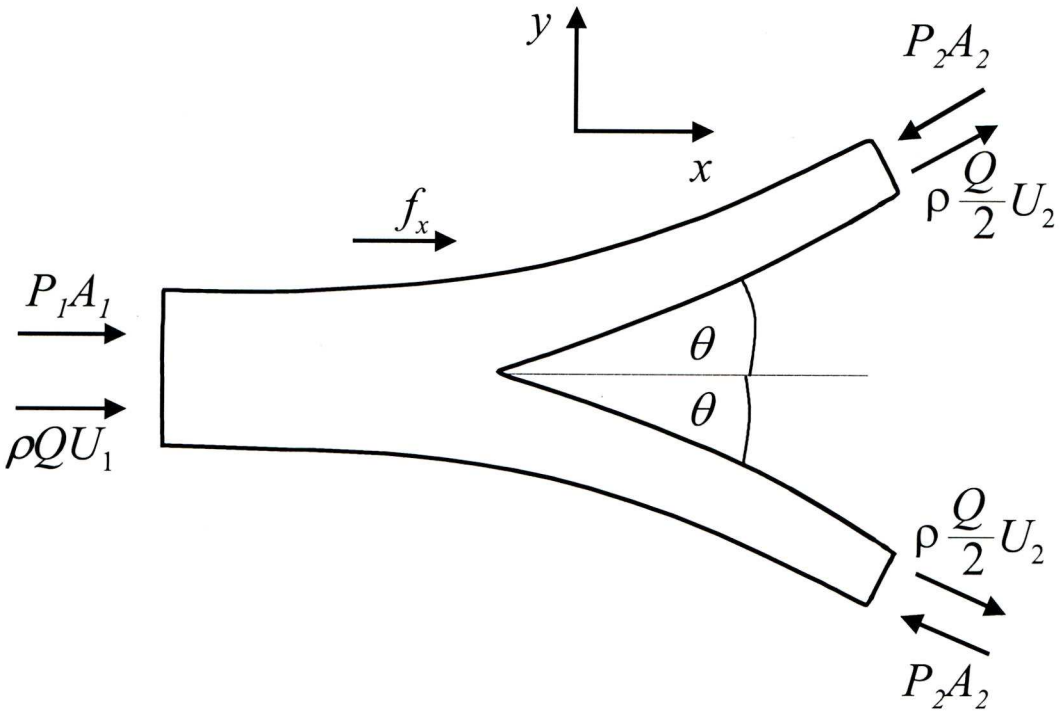

Figure 9.3: Geometry and forces acting on a bifurcated stent-graft.

9.4 Methods

The experimental model was machined using aluminium tube, joined with metal-loaded epoxy resin to form a bifurcation. The main trunk internal diameter was 30 mm, and wall thickness, 4 mm. We thinned a segment 30 mm long to 0.1 mm wall thickness on the main trunk. The thinned segment increased the level of strains locally, so the strain could be easily measured. Two strain gauges were bonded onto this section. After calibrating the strain gauges, the model was placed onto the same pulsatile flow system as described in chapter 8. The longitudinal haemodynamic force was then measured, and converted to Newtons. The pulsatile flow system could mimic human infrarenal blood flow. The pressure and flow settings were generated from elderly patient blood pressure and infrarenal blood flow. The viscosity of the viscous fluid was the same as that of normal

human blood serum, so the potential effect of viscosity of flow could be eliminated. Details of the methods are described in Chapter 5.

9.5 Results

Five experiments were carried out with the same flow rate of 1.5 l/min, heart rate of 60 beats per minute but different pressure waveforms.

The average flow and pressure waveforms and net force f_x or LF for all the five experiments are shown in Figures 9.2 (A, B, C), 9.3 (A, B, C), 9.4 (A, B, C), 9.5 (A, B, C) and 9.6 (A, B, C). Each waveform was averaged over 590 cardiac cycles.

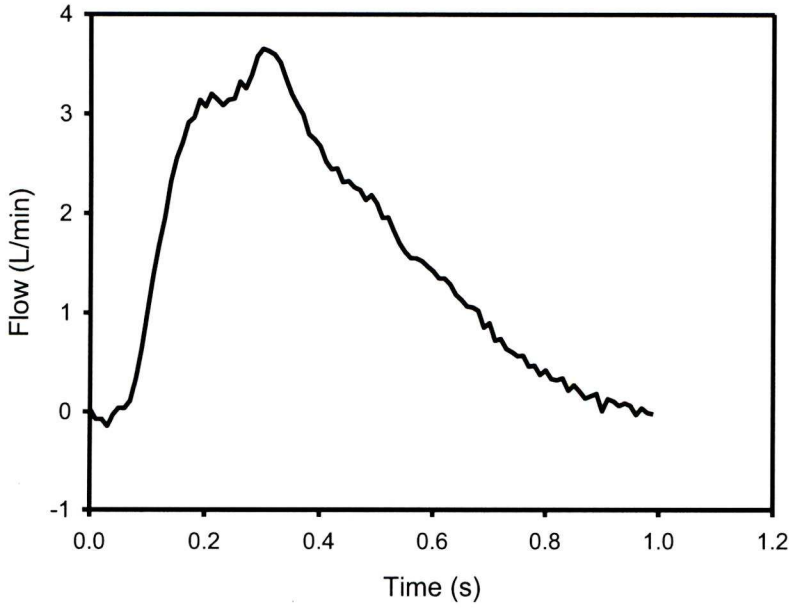

Figure 9.2A: Flow waveform in test run 1

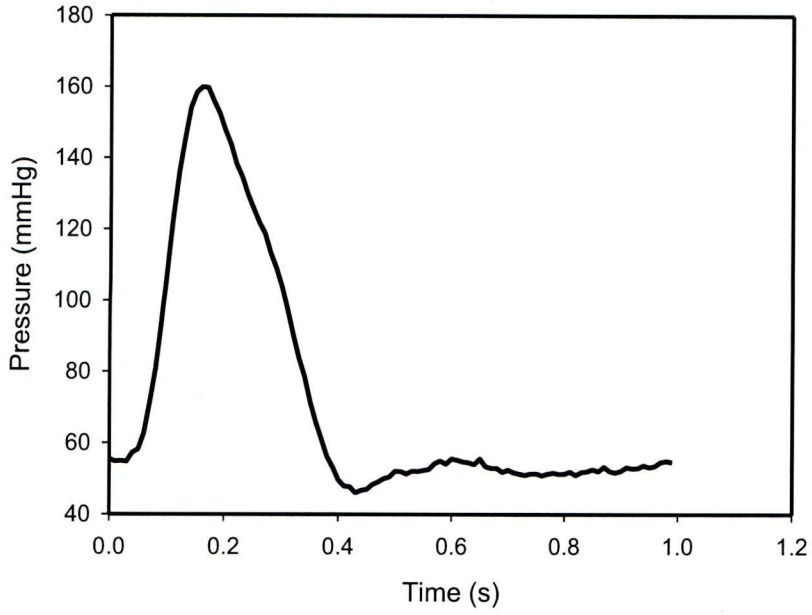

Figure 9.2B: Pressure waveform in test run 1

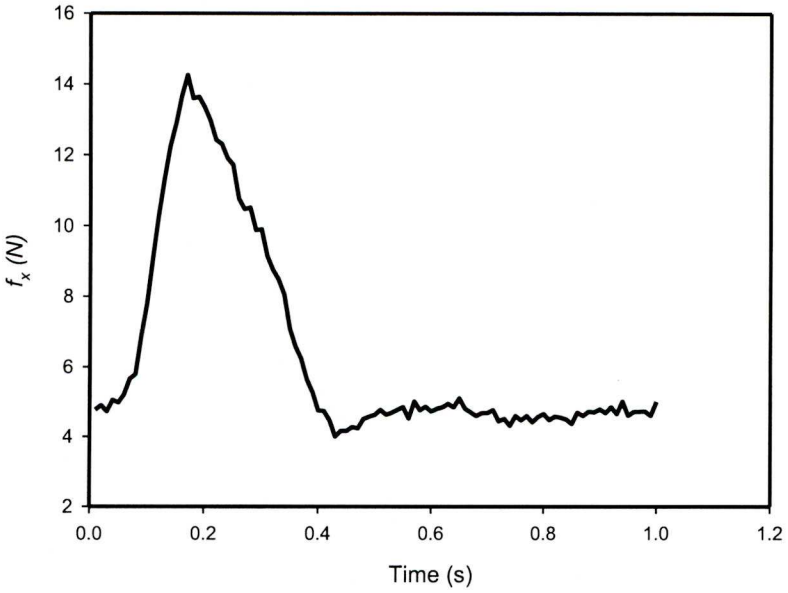

Figure 9.2C: Measuring the net force f_x or LF in test run 1

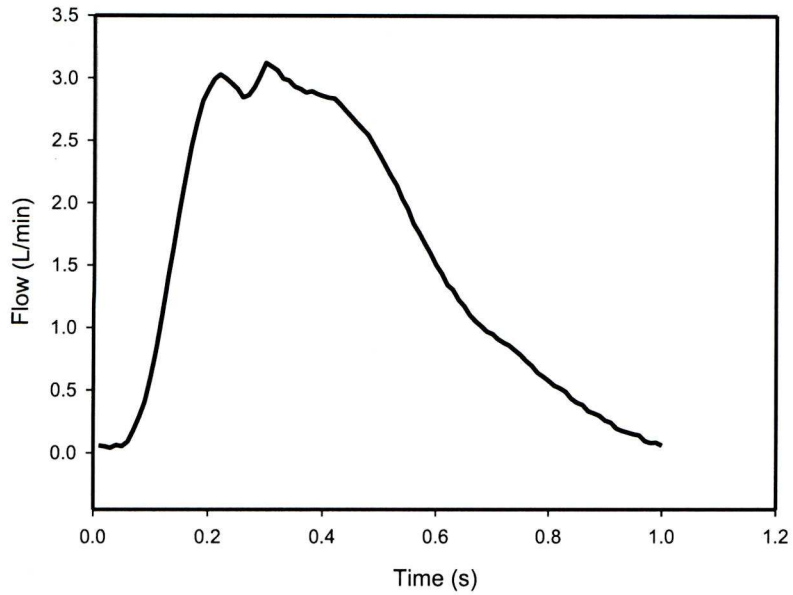

Figure 9.3A: Flow waveform in test run 2

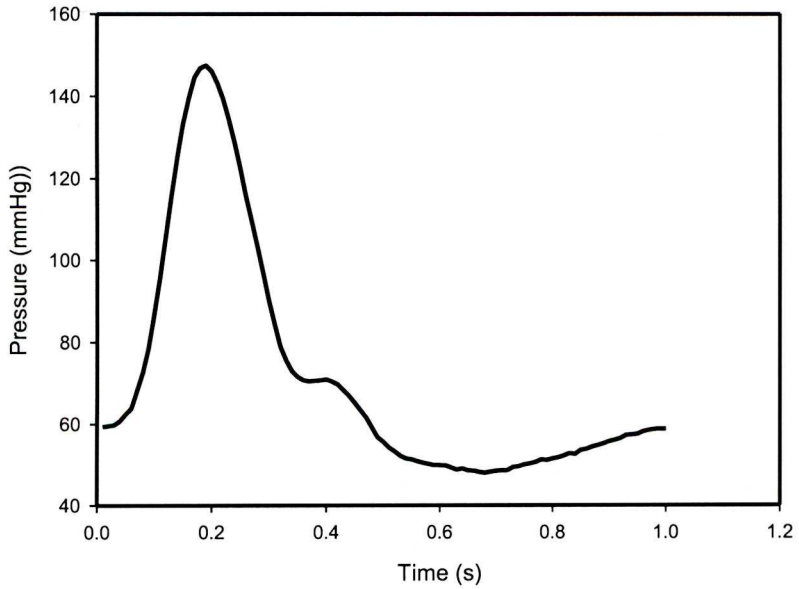

Figure 9.3B: Pressure waveform in test run 2

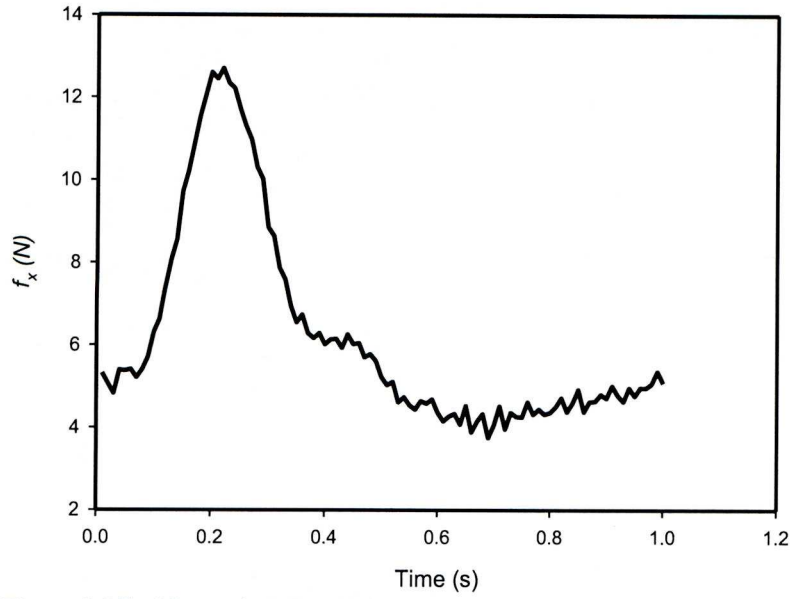

Figure 9.3C: Measuring the net force f_x or LF in test run 2

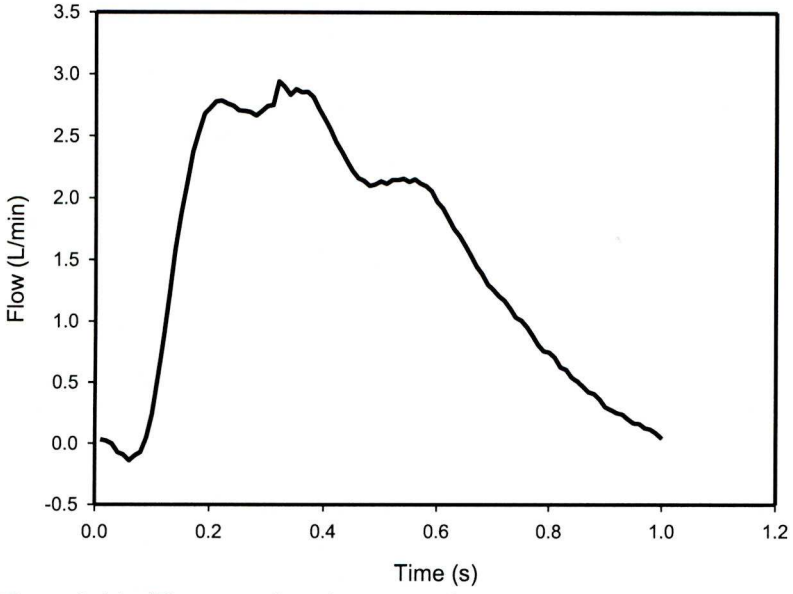

Figure 9.4A: Flow waveform in test run 3

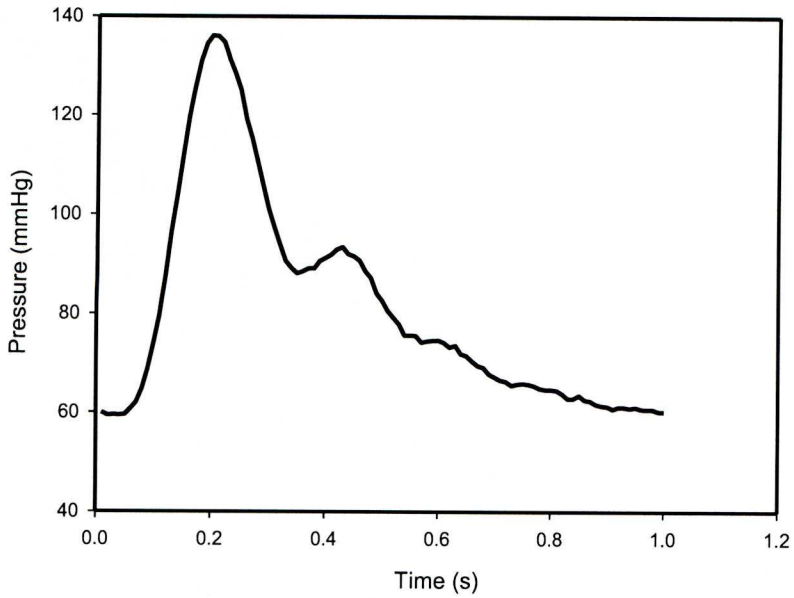

Figure 9.4B: Pressure waveform in test run 3

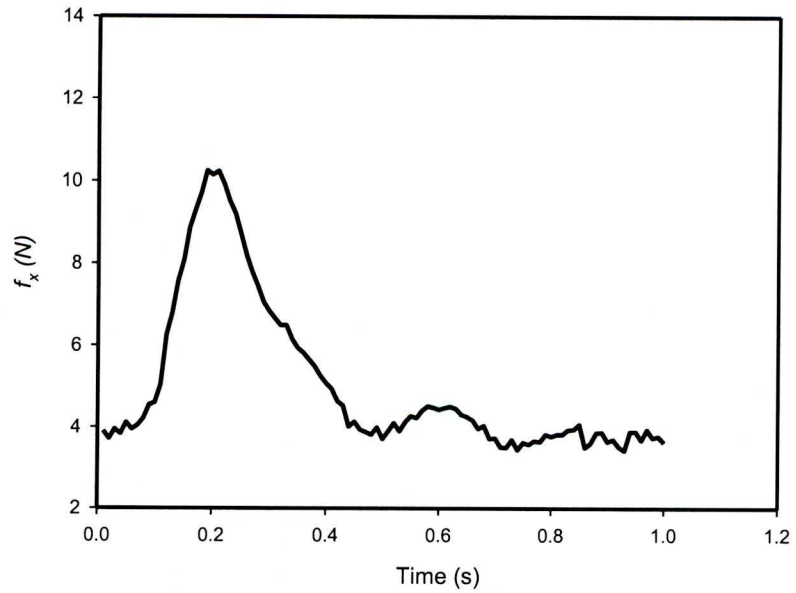

Figure 9.4C: Measuring the net force f_x or LF in test run 3

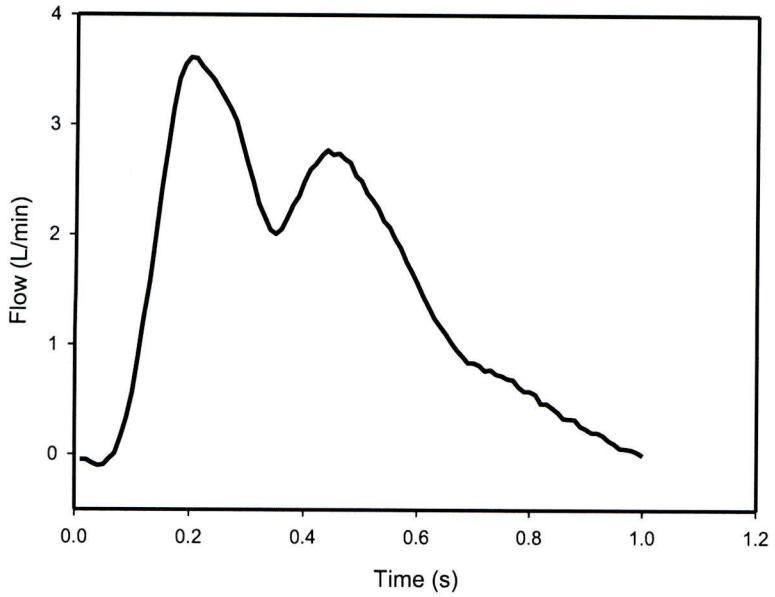

Figure 9.5A: Flow waveform in test run 4

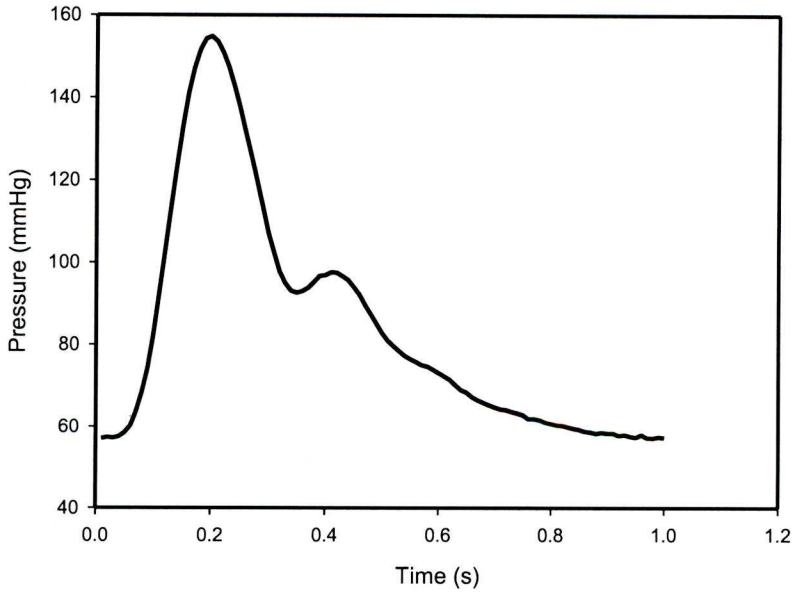

Figure 9.5B: Pressure waveform in test run 4

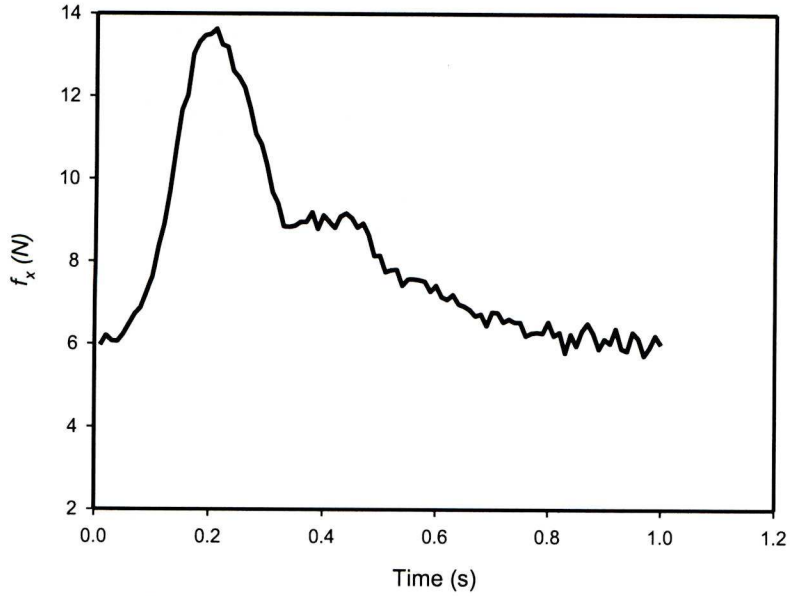

Figure 9.5C: Measuring the net force f_x or LF in test run 4

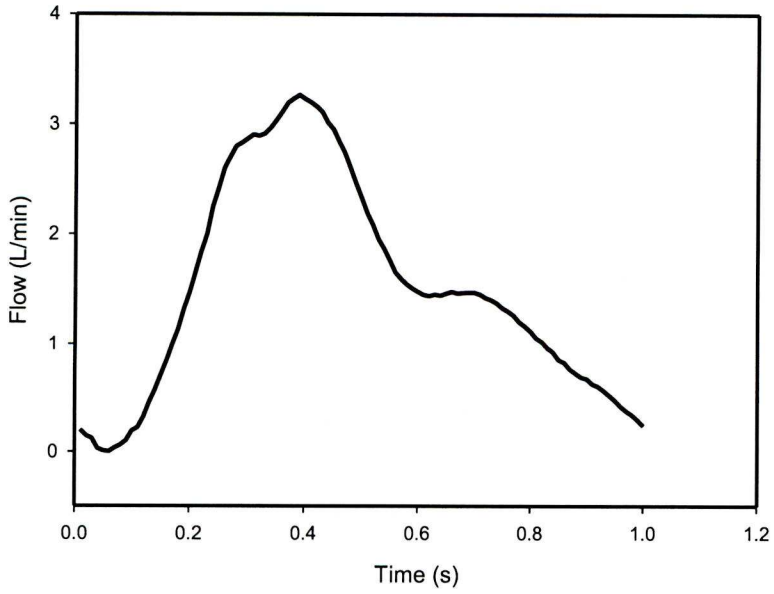

Figure 9.6A: Flow waveform in test run 5

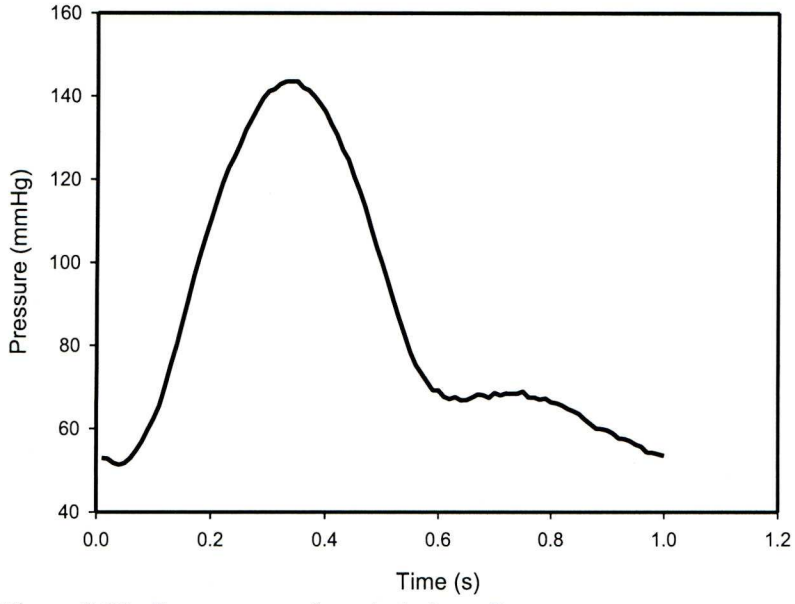

Figure 9.6B: Pressure waveform in test run 5

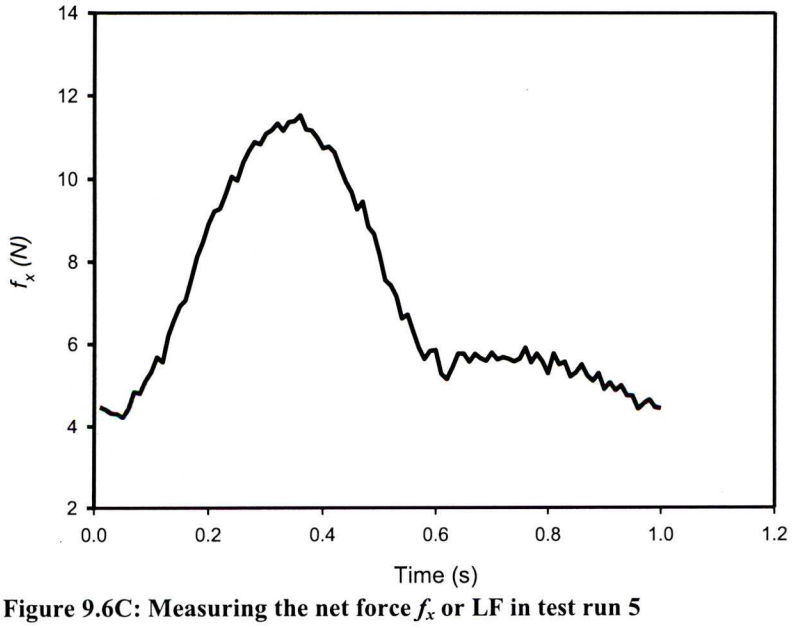

Figure 9.6C: Measuring the net force f_x or LF in test run 5

Figure 9.7 shows the measured f_x waveform as well as the theoretical values calculated from eqn. 9.2 using the actual recorded pressure and flow waveforms. The force and pressure waveforms appear to be almost in phase indicating that pressure has a greater influence on the measured forces than the flow. It can be seen from Figure 9.7 that the measured forces were greater than those calculated

from equation 9.2. The differences between measured and calculated forces expressed as a percentage of the measured values are shown in Figures 9.8, 9.9, 9.10, and 9.11.

The range of the differences was from about 6 to 18% of the measured values.

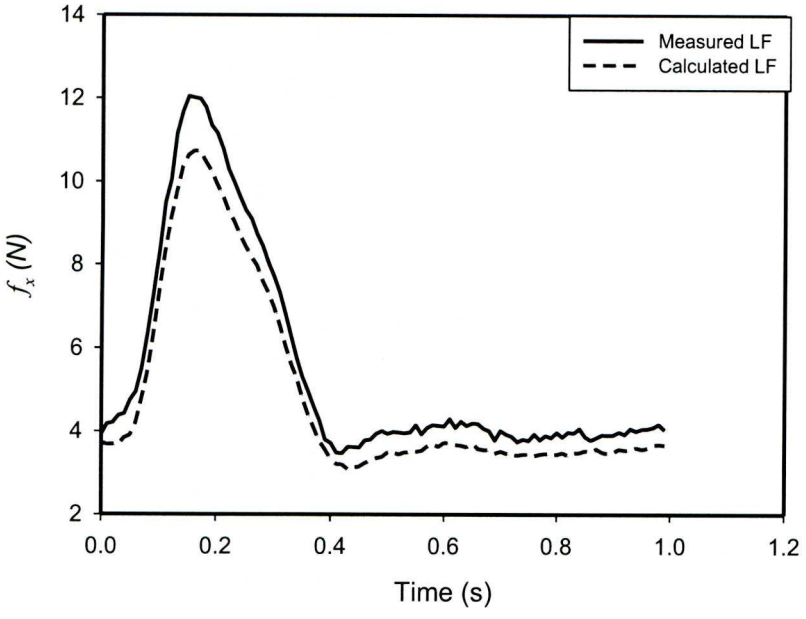

Figure 9.7: Differences between measured and calculated f_x or LF.

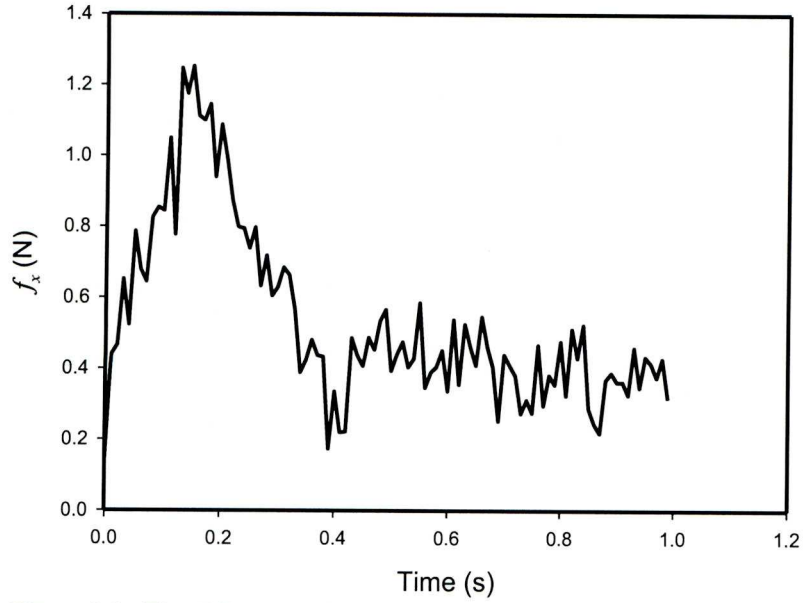

Figure 9.8: The difference between measured and calculated LF expressed as a percentage of the measured values in test run 1.

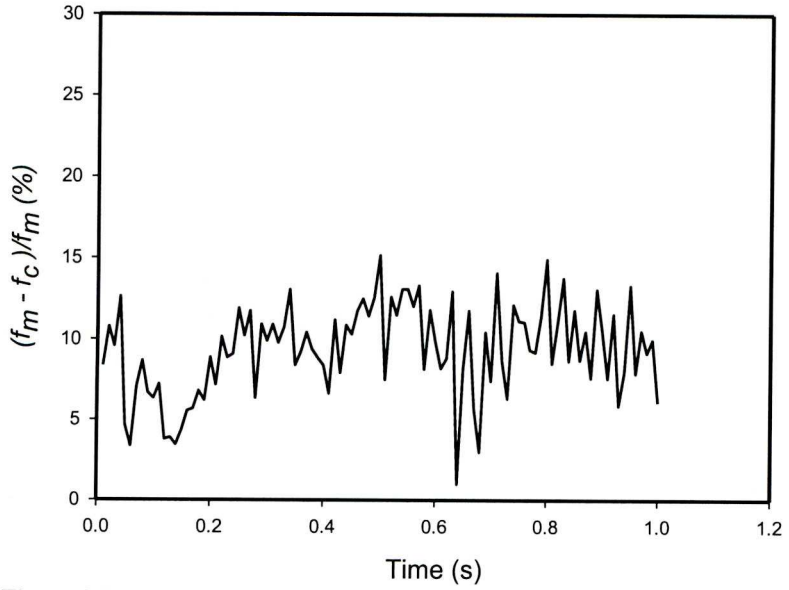

Figure 9.9: The difference between measured and calculated LF expressed as a percentage of the measured values in test run 2.

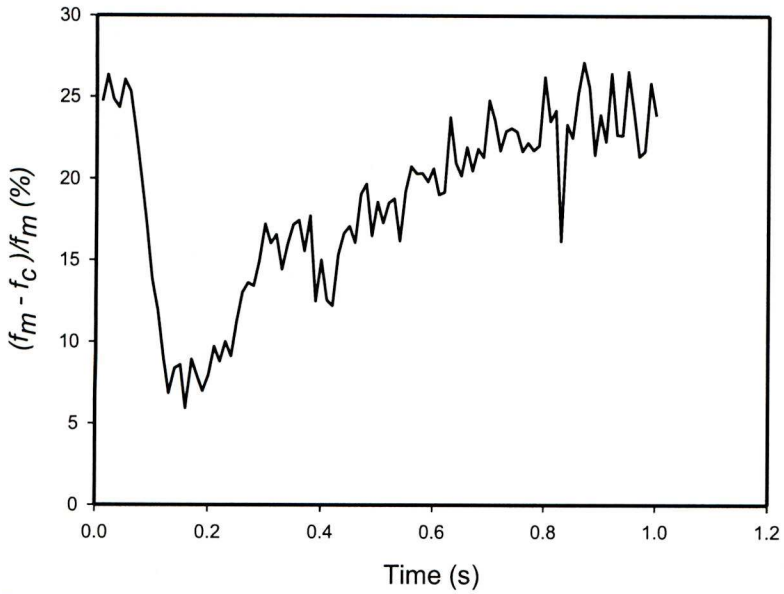

Figure 9.10: The difference between measured and calculated LF expressed as a percentage of the measured values in test run 3.

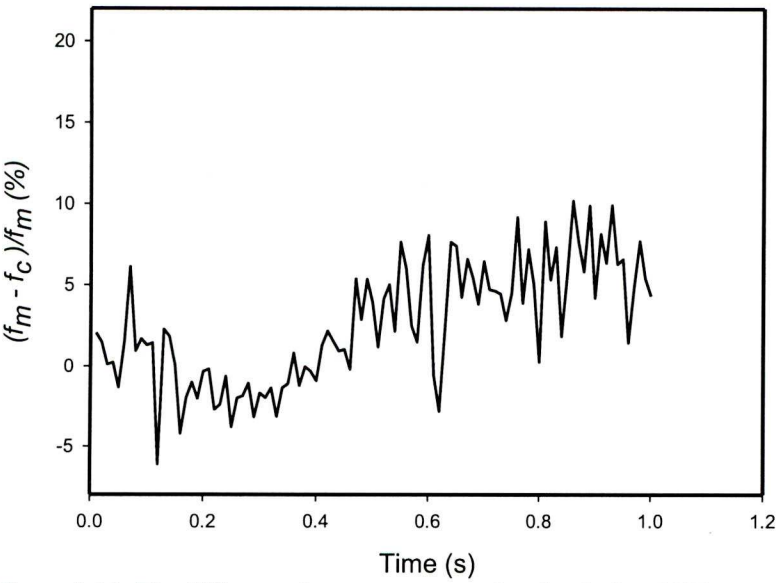

Figure 9.11: The difference between measured and calculated LF expressed as a percentage of the measured values in test run 4.

9.6 Discussion

One of the most important complications affecting the long term success of endovascular repair of aortic aneurysms is stent-graft migration; that is, movement of a stent-graft relative to the vascular anatomy, after complete deployment. Stent-grafts depend on a number of factors such as radial force, columnar strength and the presence of hooks or barbs to remain stable in position. Since they are not sutured to the aortic wall, stent-grafts are susceptible to migration. This has the potential to cause attachment-site endoleak and even a consequent aneurysm rupture (Mohan et al, 2002; Alimi et al 1998; Torsello et al 1998; Lumsden et al, 1995). A deployed stent-graft constantly faces physiological forces that tend to cause stent-graft migration and therefore stent-grafts should be designed to resist such migration. The fixation strength of commercial stent-grafts has been measured by several authors. The longitudinal force LF required to completely displace a stent-graft from an aorta has been found to range from 4.5 N to over 26 N depending on the design of stent-graft (Resch, et al, 1999; Veerapen et al, 2003).

The one-dimensional model (equation 9.2) was derived using a number of simplifying assumptions about the fluid and the geometry of the bifurcation. Morris et al (Morris et al, 2004) and Li and Kleinstreuer (Li et al, 2006) have carried out computational fluid dynamic studies of pulsatile flow in bifurcated devices and shown that blood pressure had the most effect on LF. Blood flow did not affect LF significantly. Li and Kleinstreuer (Li et al, 2006) also found that the shape of the pressure waveform was a significant factor. Pressure waveforms with high systolic slope produced higher LF than those with lower systolic slopes. This was attributed to large flow accelerations which affected the LF acting on the device.

Using a gramometer, Volodos et al (Volodos et al, 2003) measured LF in a tubular, non-bifurcated stent-graft subjected to pulsatile flow of water. More recently Sutalo et al. measured LF in an acrylic model of a bifurcated stent-graft under steady flow of water (Sotalo et al, 2005). The LF was measured by means of a load cell attached to the model and found good agreement with the predictions of the simple one-dimensional model.

This study shows that the measured LF is in relatively good agreement with the simple one-dimensional steady inviscid model. Figure 9.8-9.11 show the difference expressed as a percentage between measured and calculated LF. It can be seen that the maximum difference occurs during the mid-systolic phase of the pressure waveform. To obtain an estimate of the influence of the viscosity of the fluid, the pulsatility of the flow and the momentum forces, we first evaluate the pressure forces from the first two terms of equation 1, i.e., $P_1A_1 - 2P_2A_2\cos\theta$. This is then subtracted from the measured LF. The viscosity, the momentum and pulsatility therefore contributes approximately 0.2 to 1.2N to the measured LF, which ranged from about 4 to 12 N.

In this experiment, two strain gauges connected in the half-bridge circuit were used (Figure 5.19). The advantage over a single active strain gauge in a quarter-bridge configuration is greater sensitivity. However, the disadvantage for this half-bridge (and also the quarter-bridge configuration) is that the thermal effects do not cancel out and the output is therefore susceptible to temperature changes. To minimize the thermal effects, a low supply voltage of 2.5V was used, and the bridge completion resistors consisted of high stability precision resistors (S350, 1

ppm/°C, Vishay Measurements Group UK, Basingstoke, UK). Since the output could be affected by thermal zero drift, this was monitored before and after each measurement. This was achieved by isolating the stent-graft model from any pressure load by closing the three ball valves at the inlet and outlets and opening the pressure port to atmosphere. Any drift was zeroed using the bridge balance. Provided that the strain gauge voltage supply and the instrumentation amplifier were switched on at least 2 hours prior to the experiment to allow thermal equilibrium to be reached, the zero drift over the duration of the experiment was found to be $< \pm 5$ mV (corresponding to ± 0.16 N).

The measured LF in this experiment is strongly pressure dependent. In the pulsatile pressure condition, the LF can reach 12 N at 160 mmHg pressure. This is much greater than most of the measured proximal fixation strengths from previous chapters. However, clinically, stent-graft migration has only happened from under 3% to 28% (Tonnessen et al. 2005; Zarins et a. 2003; van Herwaarden et al. 2007). So it is fair to assume that other factors such as fixation strength from the distal seal zone and bifurcation for some design of stent-graft, must have contributed to the overall fixation strength.

9.7. Summary

In summary, the longitudinal force acting on a stent-graft can be determined experimentally, using an instrumented device. LF is strongly dependent on pressure. The fluid viscosity, momentum and pulsatility contribute between 6 and 18% of the total LF. These results confirm that under certain conditions, LF can

exceed the fixation force of some of the current endovascular stent-grafts and may therefore lead to distal migration and its potentially serious consequences.

CHAPTER 10

CONCLUSIONS, IMPLICATIONS OF FINDINGS AND SUGGESTIONS FOR FURTHER STUDY

Endovascular aneurysm repair is by now a well-established, evidence based treatment of choice which has dramatically changed the overall approach to AAA repair. With improvement in stent-graft design and more clinical experience gained, the complications of EVAR have fallen significantly in recent years. Despite the improvement in overall outcomes of EVAR, the long term results are still controversial. EVAR is associated with its own unique problems after implantation and those problems are largely not understood. Endoleak and stent-graft migration are the two most significant complications leading to EVAR failure. It is vitally important to understand these two phenomena to enable future improvement of stent-graft design. The long term durability of EVAR will continue to be challenged as long as these two complications remain unresolved. Since this research project is focused on these two most important areas, the results have significant implications for clinical practice and future studies.

The study of relationship between optimal oversizing and proximal fixation strength in EVAR has revealed that the oversizing has significant impact on stent-graft proximal fixation strength. In stent-graft with hooks and barbs, the maximal force was reached at oversizing by 20%; and 30% in stent-graft without hooks and

barbs. Further oversizing will not bring further benefit in proximal fixation strength. The barbs increase the overall proximal fixation strength. These results support the clinical findings in stent-graft with hooks and barbs, and clarify the needed for oversizing to maximize the proximal fixation strength. Migration is commonly seen as a late complication after EVAR. It is the result of pulsatile longitudinal haemodynamic force acting on the implanted stent-graft over a period of time, often years. In future studies, it would be ideal to test migration in a more realistic model of the endovascular environment, in accelerated rates far higher than the human endovascular environment; the goal is to compress the effects of years in the human circulation, into a few months or even days of testing in laboratory settings.

The study to compare the proximal fixation strength between the standard and fenestrated stent-graft discovered the mode of stent-graft migration is actually in two phases. Phase one is due to the barbs embedding into the aortic wall with migration by a few millimetres which require much smaller force. Phase two is when the full fixation strength of the device has been reached. These findings have implications in future Zenith stent-graft designs, in particular in fenestrated stent-graft.

The degree of movement in phase one migration is unlikely to cause serious consequences with the majority of standard stent-grafts. However, with a fenestrated stent-graft, migration of even this magnitude can result in distribution of shear forces to the interface between the target vessel stent and the fenestrated body of the stent-graft. The stents used in fenestrated EVAR are not primarily designed to withstand the force causing phase one migration.

This means their strength may not be sufficient to withstand this force, resulting in crushing or even fracture of stents, and possible occlusion of the target vessel. Clinically, it is important to select stents which can withstand force sufficient to potentially cause phase one migration, during fenestrated EVAR. The stent with open cell structure should best be avoided for this reason.

The study also found that the fenestrated stent-graft configuration confers a greater proximal fixation than conventional devices. It is clear that the extra portion of the strength is produced by the fenestration stent. But how much strength is from the fenestration stent alone is still unknown and warrants further study. Furthermore, different commercially available stents such as Palmaz, genesis, atrium, jomed or different structured stents like open and closed cell stent may produce different strengths, so by further study into fixation strength testing this strength in different stents, the designed proximal fixation strength in fenestrated stent-graft may be increased further, therefore reducing the chance of migration.

It is routine clinical practice for stent-graft oversizing of the aortic neck, to obtain a proximal seal. But it is not clear how much oversizing is needed for an optimal seal. Furthermore, whether the same percentage of oversizing is required to obtain a seal in different seal zone lengths is not clear.

The study into the optimal degree of oversizing required for an effective seal in standard and fenestrated EVAR, revealed that the percentage of oversize needed

to secure a seal is inversely related to seal zone length both in fenestrated and standard stent-graft. The shorter the seal zone length, the more oversize is required to achieve proximal seal. For fenestrated EVAR with bare stent, a seal can be achieved at aortic neck length as short as 5 mm. The clinical implications of these results suggest that percentage of oversizing should not be the same for different aortic neck lengths. In general, the longer the neck length, the less oversizing is needed for a secure proximal seal. As stated above, in fenestrated EVAR, with bare stent, this can achieve a seal at neck length of 5 mm, at shortest. A covered stent should be considered for neck length shorter than 5 mm.

However, since there is no aneurysm sac in this study, the pressure difference between the intraluminal and extraluminal is at its greatest. This may have exaggerated the endoleak at certain aortic neck length and pressure setting. Furthermore, the experiments studied the standard and fenestrated stent-graft at different aortic neck length settings, so the results were not directly comparable between these two experiments. Further study is need in a model with an aneurysm sac, so it will closer mimic the situation in vivo. More study is needed to compare between standard and fenestrated stent-graft in exactly the same settings, in order to elucidate the reason why fenestrated stent-graft can obtain a seal in shorter aortic neck lengths.

The longitudinal haemodynamic force is the force created by blood flow (in the aorta), this will tend to push the stent-graft distally, to cause stent-graft migration. An implanted stent-graft on the other hand, should have designed fixation strength exceeding the longitudinal haemodynamic force, to prevent migration occurring. In the study of measurement of pulsatile haemodynamic forces in a model of a

bifurcated stent graft for abdominal aortic aneurysm repair, we measured the LF in a bifurcated stent-graft model. The results suggest that the LF is strongly dependent on pressure. The fluid viscosity, momentum and pulsatility contribute between 6% and 18% of the total LF. These results confirm that under certain conditions, LF can exceed the fixation force of some of the current endovascular stent-grafts and may therefore allow migration, proximal Type I endoleak, and other serious consequences. Further study is needed to determine the LF more accurately in vivo.

All the findings from this research have led to the conclusion that proximal oversizing has a significant effect on the proximal fixation strength. To achieve maximal proximal fixation strength, 20% oversizing is needed in stent-graft with hooks and barbs and 30% oversizing is needed in stent-graft without hooks and barbs. The barbs increase the overall proximal fixation strength. Stent-graft migration occurs in two phases. Phase one is due to the barbs embedding into the aortic wall with migration of a few millimetres. Phase two is when the full fixation strength of the device has been reached. The fenestrated stent-graft configuration confers a greater proximal fixation than standard devices. In standard and fenestrated EVAR, a different percentage of oversizing is needed to secure a proximal seal in different aortic neck lengths. Shorter aortic neck lengths require more oversizing to secure a seal. In fenestrated EVAR with bare stent, a seal can be achieved at aortic neck length as short as 5 mm. The LF is strongly dependent on pressure. LF can exceed the fixation force of some of the current endovascular stent-grafts and may therefore allow migration, proximal Type I endoleak and aneurysm rupture.

BIBLIOGRAPHY

Adams D C , Tulloh B R, Galloway S W, Shaw E, Tulloh A J, Poskitt K R. (1993). "Familial Abdominal Aortic-Aneurysm - Prevalence and Implications for Screening" Eur J of Vasc Surg; 7(6): 709-12.

Adamson J, Powell J T, Greenhalgh RM. (1992). "Selection for Screening for Familial Aortic-Aneurysms" British J of Surg; 79(9): 897-98.

Ahn S S, Rutherford R B, Johnston K W, May J, Veith FJ, Baker JD, Ernst CB, Moore WS. : (1997). "Reporting standards for infrarenal endovascular abdominal aortic aneurysm repair." Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery /International Society for Cardiovascular Surgery; J Vasc Surg; 25: 405-10,

Ailawadi G B K, Lu G, Roelofs K J, Ford J W , Hannawa K K, Bishop K, Thanaporn P, Henke P K, Stanley J C, Upchurch G R (2003). "A nonintrinsic regional basis for increased infrarenal aortic MMP-9 expression and activity." J Vasc Surg; 37: 1059-66.

Akkersdijk G, A De Vries J P, (1992). "Het aneurysma aortae abdominalis als nevenbevinding bij echogra.schonderzoek vzn het abdomen." Ned Tijdschr Geneeskd; 136: 1907-13.

Albertini J, Kalliafas S, Travis S, Yusuf S W, Macierewicz J A, Whitaker S C, Elmarasy NM, Hopkinson BR . (2000). "Anatomical risk factors for proximal perigraft endoleak and graft migration following endovascular repair of abdominal aortic aneurysms". Eur J Vasc Endovasc Surg; 19(3): 308-12.

Alimi, Y S, Chakfe, N, Rivoal, E, Slimane, K K , Valerio N, Riepe, G, Kretz, J G, Juhan, C. (1998) "Rupture of an abdominal aortic aneurysm after endovascular graft placement and aneurysm size reduction. J Vasc Surg;, 28, 178–83.

Allardice J T, Allwright G J, Wafula JM, Wyatt AP (1988). "High Prevalence of Abdominal Aortic-Aneurysm in Men with Peripheral Vascular Disease - Screening by Ultrasonography", British J Surg; 75(3): 240-42.

Al-Zahrani H A, Rawas M, Maimani A, Gasab M, Aba al Khail BA. (1996). "Screening for abdominal aortic aneurysm in the Jeddah area, western Saudi Arabia". Cardiovascular Surgery (London, England). 4(1): 87-92.

Amparo E G, Hoddick W K, Hricak H, Sollitto R, Justich E, Filly RA, Higgins CB. (1985). "Comparison of magnetic resonance imaging and ultrasonography in the evaluation of abdominal aortic aneurysms" Radiology; 154(2): 451-56.

Anderson J L, Berce M, Hartley D. (2001). "Endoluminal aortic grafting with renal and superior mesenteric artery incorporation by graft fenestration." J Endovasc Ther; 8: 3–15.

Andrews SM, Cuming R, Macsweeney ST, Barrett NK, Greenhalgh RM, Nott DM. (1995). "Assessment of feasibility for endovascular prosthetic tube correction of aortic aneurysm" Br J Surg;82:917-9.

Appleberg M (1994). "Abdominal aortic aneurysms: pathogenesis diagnosis and management". Mod Med; 37: 54-63.

Arko, FR, Kostantinos AF, and Seidel SA. How many patients with infrarenal aneurysms are candidates for endovascular repair? The Northern California experience. J. Endovasc. Ther. 11:33–40, 2004;

Armon MP, Yusuf SW, Latief K, Whitaker S C, Gregson R H and Wenham P W Hopkinson BR. (1997). "Anatomical suitability of abdominal aortic aneurysms for endovascular repair", Bri J Surg; 84. 178–80.

Ashton H C, E Duffy S. A (2000). "Comparative study of the prevalence of abdominal aortic aneurysms in the United Kingdom, Denmark, and Australia." J Med Screen; 8: 46-50.

Auerbach O and Garfinkel L. (1980). "Atherosclerosis and Aneurysm of Aorta in Relation to Smoking- Habits and Age." Chest, 78(6): 805-9.

Back MR, Bandyk M, Bradner M, Cuthbertson D, Johnson BL, Shames ML, Bandyk DF. (2005). "Critical analysis of outcome determinants affecting repair of intact aneurysms involving the visceral aorta." Ann Vasc Surg; 19: 648-56.

Bayle O, Branchereau A,.Rosset E,.Guillemot E, Beaurain P and Ferdani M Jausseran JM. (1997). "Morphologic assessment of abdominal aortic aneurysms by spiral computed tomographic scanning", J Vasc Surg; 26 pp. 238–46.

Beebe H G; Kritpracha, B; Serres S; John P. Pigott,J P; Price C I; and Williams, D M. (2000), "Endograft Planning Without Preoperative Arteriography: A Clinical Feasibility Study" J Endovasc Ther, 7: (1) 81-5

Bengtsson H, Ekberg O, Aspelin P, Källerö S, Bergqvist D. (1989). "Ultrasound screening of the abdominal aorta in patients with intermittent claudication." Eur J Vasc Surg 3: 497-502.

Bengtsson H, Bergqvist D, Sternby NH. (1992). "Increasing Prevalence of Abdominal Aortic-Aneurysms - a Necropsy Study". Eur J of Surg 158(1): 19-23.

Bengtsson H, Sonesson B, Länne T, Nilsson P, Solvig J, Loren I, Bergqvist D. (1992). "Prevalence of Abdominal Aortic-Aneurysm in the Offspring of Patients Dying from Aneurysm Rupture." Br J Surg; 79(11): 1142-43.

Biancari F, Yionen K, Anttila V, Juvonen J, Romsi P, Satta J, Juvonen T. (2002): "Durability of Open Repair of Infrarenal Abdominal Aortic Aneurysm: A 15-year Follow-up Study" J Vasc Surg 35(1): 87-93

Bicknell CD, Cheshire NJW, Riga CV, Bourke P, Wolfe JHN, Gibbs RG, Jenkins MP, Hamady M. (2009). "Treatment of complex aneurysmal disease with fenestrated and branched stent grafts". Eur J Vasc Endovascular Surg; 37(2): 175-81.

Bicknell CD, Cowan AR, Kerle MI, Mansfield AO, Cheshire NJ, Wolfe JH. (2003). "Renal dysfunction and prolonged visceral ischaemia increase mortality rate after suprarenal aneurysm repair." Br J Surg; 90(9): 1142-6.

Blankensteijn J D, Lindenburg F P, Van Der Graaf Y, and Eikelboom B C. " Influence of Study Design on Reported Mortality and Mobydity Rates after Abdominal Aortic Aneurysm Repair" British J of Surgery 85: 1624-30.

Blum U, Voshage G, Lammer J, Beyersdorf F, Töllner D, Kretschmer G, Spillner G, Polterauer P, Nagel G, Hölzenbein T . (1997). "Endoluminal stent-grafts for infrarenal abdominal aortic aneurysms." N Engl J Med; 336: 13–20.

Boll, A. P Verbeek AL, van de Lisdonk EH, van der Vliet JA. (1998). "High prevalence of abdominal aortic aneurysms in a primary care screening programme." British J of Surgery 85: 1090-94..

Bower T C, Cherry K. J, Jr, Pairolero PC. (1989). "Unusual manifestations of abdominal aortic aneurysms." The Surg Cl N Am 69(4): 745-54.

Boyle J R M, Crowther E, Wills M, Bell A, Thompson,M.M. (1998). "Doxycycline inhibits elastin degradation and metalloproteinase production in a model of aneurysmal disease." J Vasc Surg 27: 354-61.

Boyle JR, Goodall S, Thompson JP, Bell PR, Thompson MM. (2000). "Endovascular AAA repair attenuates the inflammatory and renal responses associated with conventional surgery". J Endovasc Ther; 7:359–71.

Boyle JR, Thompson JP, Thompson MM, Sayers RD, Smith G, Bell PR . (1997). "Improved respiratory function and analgesia control after endovascular AAA repair." J Endovasc Surg; 4: 62–5

Bradbury A W, Adam D J, Makhdoomi K R, Stuart W P, Murie J A, Jenkins A M and Ruckley C V. (1998) "A 21-year experience of abdominal aortic ameurysm operaion in Edinburgh" Br J Surg 85: 645-7

Brady A R S T, Greenhalgh RM, Powell JT (2003). "For the UK Small Aneurysm Trial Participants. Cardiovascular risk factors and abdominal aortic aneurysm expansion: only smoking counts." Br J Surg; 90: 491–92.

Brady A R, Fowkes F G, Thompson S G and Powell J T. (2001) "Aortic aneurysm diameter and risk of cardiovascular mortality." Arterioscler Thromb Vas Biol 21:(7) 1203-7.

Brady AR, Greenhalgh RM, Powell JT (2003). "For the UK Small Aneurysm Trial Participants.Cardiovascular risk factors and abdominal aortic aneurysm expansion: only smoking counts". Br J Surg;, 90: 491–2.

Brewster DC, Darling RC, Raines JK, Sarno R, O'Donnell TF, Ezpeleta M, Athanasoulis C. (1977). "Assessment of abdominal aortic aneurysm size." Cardiovasc Surg 56: 164–9.

Browne T.F., Hartley D., Purchas S. Rosenberg M, Van Schie G, Lawrence-Brown M. (1999). "A fenestrated covered suprarenal aortic stent." Eur J Vasc Endovasc Surg; 18: 445–9.

Budd J F, D Carter P. (1989). "A study of the mortality of ruptured abdominal aortic aneurysms in a district community." Eur J Vasc Surg 3: 351-63.

Buth J, Laheij RJ. (2000). "Early complications and endoleaks after endovascular abdominal aortic aneurysm repair: report of a multicenter study." J Vasc Surg; 31: 134–46.

Cannon D J,. Casteel L, Read RC. (1984). "Abdominal Aortic-Aneurysm, Leriches Syndrome, Inguinal Herniation, and Smoking." Arch Surg 119(4): 387-89.

Cao P, Rango P De, Verzini F, Parlani G (2010). "Endoleak after endovascular aortic repair: classification, diagnosis and management following endovascular thoracic and abdominal aortic repair" J Cardiovasc Surg: 51(1); 53-69

Cao P, Verzini F, Zannetti S, De Rango P, Parlani G and. Lupattelli L Maselli A. (2002). "Device migration after endoluminal abdominal aortic aneurysm repair: analysis of 113 cases with a minimum follow-up period of 2 years." J Vasc Surg 35 (2) pp. 229–35.

Carpenter JP, Baum RA, Barker CF, Golden MA, Velazquez OC, Mitchell ME, Fairman RM. (2002). "Durability of benefits of endovascular versus conventional abdominal aortic aneurysm repair." J Vasc Surg; 35:222–8.

Carpenter JP, Baum RA, Barker CF, Golden MA, Mitchell ME, Velaquez OC, et al. (2001). "Impact of exclusion criteria on patient selection for endovascular abdominal aortic aneurysm repair." J Vasc Surg; 34: 1050-4, 2001

Carpenter, JP., Anderson WN, Brewster D, Kwolek CC, Makaroun M, and Martin J. "Multicenter pivotal trial results of the Lifepath System for endovascular aortic aneurysm repair". J. Vasc. Surg. 39:34–43, 2004.

Castleden W M and Mercer J. C. (1985). "Abdominal Aortic-Aneurysms in Western Australia - Descriptive Epidemiology and Patterns of Rupture." Br J Surg 72(2): 109-112.

Cau J, Ricco J.B, Marchand C, Lecis A, Habbibeh H, Guillou M, Febrer G and Bossavy J.P. (2006). "Total Laparoscopic Aortic Repair for Occlusive and Aneurysmal Disease: First 95 Cases", Eur J Vasc Endovasc Surg; 31: 567–74

Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, Matsumura JS, May J, Veith FJ, Fillinger MF, Rutherford RB, Kent KC. (2002). "Reporting standards for endovascular aortic aneurysm repair." J Vasc Surg; 35: 1048-60,

Cheatle T R and Scurr J. H (1989). "Abdominal aortic aneurysms: a review of current problems." Br J Surg 76(8): 826-9.

Chiesa R, Marone EM, Brioschi C, Frigerio S, Tshomba Y, Melissano G. "2006" "Open repair of pararenal aortic aneurysms: operative management, early results, and risk factor analysis". Ann Vasc Surg; 20(6): 739-46.

Coggon D, Winter P, Martyn C, Inskip H. (1996). "Contrasting epidemiology of aortic aneurysm and peripheral vascular disease in England and Wales." BMJ 312: 948.

Collin J. (1996). " The Oxford Screening Program for aortic aneurysm and screening first-order male siblings of probands with abdominal aortic aneurysm." Ann N Y Acad Sci. 1996 Nov 18;800:36-43

Collin J, Murie JA. (2001). "Endovascular treatment of abdominal aortic aneurysm: a failed experiment." Br J Surg; 88: 1281–2.

Collin, J. (1988). "The epidemiology of abdominal aortic aneurysm." Br J Hosp Med 39: 64-7.

Collin, J. (1990). "A Proposal for a Precise Definition of Abdominal Aortic- Aneurysm - a Personal View." J Cardiovasc Surg 31(2): 168-9.

Conners MS, Sternbergh WC, Carter G. Tonnessen BH, Yoselevitz M, Money SR. (2003). "Endograft migration one to four years after endovascular abdominal aortic aneurysm repair with the AneuRx device: a cautionary note". J Vasc Surg; 36(3): 476 – 84.

Cook T A. and Galland R B. (1996). "A prospective study to define the optimum rescreening interval for small abdominal aortic aneurysm." Cardiovasc Surg 4(4): 441-4.

Corine van Marrewijk, Jacob Buth, Peter L. Harris, Lars Norgren, André Nevelsteen, and Michael G. Wyatt. (2006). "Significance of endoleaks after endovascular repair of abdominal aortic aneurysms: The EUROSTAR experience" J Vasc Surg; 35: (3) 461-73

Crawford C M,. Hurtgen-Grace K, Talarico E, Marley J. (2003). "Abdominal aortic aneurysm: an illustrated narrative review." J Manipulative and Physiological Therapeutics 26(3): 184-95.

Crawford E S, Saleh S A, Babb J W, P S, Glaeser D H, Vaccaro P S and Silvers A. (1981) "Infrarenal abdominal aortic aneurysm: factors influencing survival after operation performed ober a 25-year perod." Ann Surg; 193(6): 699-709

Crawford ES, BeckettWC, Greer MS. (1986). "Juxtarenal infrarenal abdominal aortic aneurysm. Special diagnostic and therapeutic considerations". Ann Surg 203: 661–670.

Creech O Jr. (1966). "Endo-aneurysmorrhaphy and treatment of aortic aneurys." Ann Surg; 164(6): 935-46.

Criado FJ, Wilson EP, Wellons E, Abul-Khoudoud O, Gnanasekeram H. (2000). "Early experience with the Talent stent-graft system for endoluminal repair of abdominal aortic aneurysms." Tex Heart Inst J; 27: 128–35

Cronenwett J L, Murphy T F, Zelenock GB, Whitehouse WM Jr, Lindenauer SM, Graham LM, Quint LE, Silver TM, Stanley JC. (1985). "Actuarial analysis of variables associated with rupture of small abdominal aortic aneurysms." Surgery 98(3): 472-83.

Cuci J A, Liao S, Golub L M, Thompson RW (1998). "Pharmacologic suppression of experimental abdominal aortic aneurysms: a comparison of doxycycline and four chemically modified tetracyclines." J Vasc surg 28: 1082-93.

Curci JA, Fillinger, Naslund TC, Rubin BG; for the Excluder Bifurcated Endoprosthesis Investigators: clinical trial results of a modified Gore Excluder endograft: comparison with open repair and original device design. Ann Vasc Surg 21:328-338, 2007

Darling R, LaMuraglia D B G, Moncure A and Cambria W A R (1989). "Are familial aneurysms different ?" J Vasc Surg; 10: 650-6.

Desai, H B, Rajput A H, Uitti RJ. (1989). "Recurrent spinal cord ischemia due to abdominal aortic aneurysm--a case report." Angiology; 40: (7): 682-7.

Dias NV, Ivancev K, Resch TA, Malina M, Sonesson B (2007); "Endoleaks after endovascular aneurysm repair lead to nonuniform intraaneurysm sac pressure". J Vase Surg 46:197-203.

Dias N.V, Resch T, Malina M, Lindblad B and Ivancev K. (2001) "Intraoperative proximal endoleaks during AAA stent-graft repair:evaluation of risk factors and treatment with Palmaz stents." J Endovasc Ther; 8: (3) pp. 268–73.

Drott C, Arfvidsson B, Ortenwall P, Lundholm K. (1992). "Age-Standardized Incidence of Ruptured Aortic-Aneurysm in a Defined Swedish Population between 1952 and 1988 - Mortality- Rate and Operative Results." Br J Surg 79(2): 175-9.

Drury D, Michaels JA, Jones L, Ayiku L. (2005). "Systematic review of recent evidence for the safety and efficacy of elective endovascular repair in the management of infrarenal abdominal aortic aneurysm." Br J Surg; (8): 937-46.

Dubost, C. A., . Oeconomos,N. (1952). "Resection of the aneurysm of the abdominal aorta: Re-establishment of the continuity by a preserved human arterial graft, with result after five months." Arch. Surg; 64: 405-11.

Duthie, J. J. R. (1988). "SCREENING FOR ABDOMINAL AORTIC ANEURYSM." The Lancet; 332(8623): 1319-32.

Dzau V, Root R. (1991). "Diseases of the aorta". Harrison's principles of internal medicine; New York, Mc Graw-Hill: 1015-8.

Ecklund K, Hartnell G. G, Hughes LA, Stokes KR, Finn JP. (1994). "MR angiography as the sole method in evaluating abdominal aortic aneurysms: correlation with conventional techniques and surgery." Radiology; 192(2): 345-50.

Eickhoff J H. (1993). "Incidence of Diagnosis, Operation and Death from Abdominal Aortic-Aneurysms in Danish Hospitals - Results from a Nationwide Survey, 1977-1990." Eur J of Surg; 159(11-12): 619-23.

Elkouri S, Gloviczki P, McKusick MA, Panneton JM, Andrews J, Bower TC, Noel AA, Harmsen WS, Hoskin TL, Cherry K. (2004). "Perioperative complications and early outcome after endovascular and open surgical repair of abdominal aortic aneurysms." J Vasc Surg; 39: 497–505.

Ellis M, Powell JT, Greenhalgh RM, (1991). "Limitations of ultrasonography in surveillance of small abdominal aortic aneurysms." Br J Surg; 78: 614-6.

England A, Butterfield JS, McCollum CN, Ashleigh RJ (2008): "Endovascular aortic aneurysm repair with the Talent stent-graft: outcomes in patients with large iliac arteries." Cardiovasc Intervent Radiol 31:723-727,

EVAR trial participants. (2005). "Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial." Lancet; 365(9478): 2187–92.

EVAR trial participants. (2005). "Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial." Lancet; 365: 2179–86.

Farber E R, Farber J. L, Lippincott J B. (1995). "Development and genetic diseases. Essential pathology". Philadelphia; 125–160.

Faries PL, Briggs VL, Rhee JY, Burks Jr JA, Gravereaux EC, Carroccio A, Morrissey NJ, Teodorescu V, Hollier LH, Marin ML. (2002). "Failure of endovascular aortoaortic tube grafts: a plea for preferential use of bifurcated grafts." J Vasc Surg; 35(5): 868-73.

Fitzgerald P, Ramsbottom D, Burke P, Grace P, McAnena O, Croke DT, Collins P, Johnson A, Bouchier-Hayes D. (1995). "Abdominal Aortic Aneurysm in the Irish Population: a Familial Screening Study." Br J Surg; 82(4): 483-6.

Fowkes FG Macintyre CC, Ruckley CV. (1989). "Inverasing incidence of aortic aneurysms in England and Wales." BMJ; 298: 33-5.

Frame PS, Fryback DG, Patterson C. (1993). "Screening for abdominal aortic aneurysm in men ages 60 to 80 years. A cost effectiveness analysis." Ann Inter Med 119(5): 411-6.

Franklin I Walton LJ, Brown L, Greenhalgh RN, Powell JT. (1999). "Vascular surgical Socirty of Great Britain and Irland: non-steroidal anti-inflammatory drugs to treat abdominal aortic aneurysm." Br J Surg; 86: 707.

Franko T.J, Zajko AB, Federle MP, Makaroun MS. (2000)."Endovascular repair of abdominal aortic aneurysm with the Ancure endograft: CT follow-up of perigraft flow and aneurysm size at 6 months." J Vasc Interv Radiol; 11: 429–435.

Friedman S G, "The 50th anniversary of abdominal aortic reconstruction" J Vasc Surg; 33(4): 895-8

Fulton JJ, Farber MA, Sanchez LA, Godshall CJ, Marston WA, Mendes R, Rubin BG, Sicard GA, Keagy BA. (2006). "Effect of challenging neck anatomy on midtermmigration rates in AneuRx endografts". J Vasc Surg; 44(5): 932-7

Gilling-Smith GL, Brennan J, Harris P, Bakran A, Gould D, and McWillians R (1999) "Endotension after endovascular aneurysm repair: definition, classification, and trrategies for surveillance and intervention." J Endovasc Surg 6(4): 305-7

Goldstone J. (1993). "Aneurysms of the aorta and iliacv arteries. Vascular surgery: Acomprehensive review". M. WS. Philadelphia, WB Saunders and Co: 401-23.

Greenberg RK, Chuter TA, Sternbergh WC 3rd, Fearnot NE; Zenith Investigators. (2004). "Zenith AAA endovascular graft: Intermediate-term results of the US multicenter trial". J Vasc Surg:.39; 6: 1209-18.

Greenberg RK, Chuter TA, Cambria RP, Sternbergh WC 3rd, Fearnot NE (2008)."Zenith abdominal aortic aneurysm endovascular graft." J Vasc Surg 48:1-9.

Greenberg RK, Turc A, Haulon S, Srivastava SD, Sarac TP, O'Hara PJ, Lyden SP, Ouriel K. (2004). "Stent-graft migration: a reappraisal of analysis methods and proposed revised definition." J Endovasc Ther; 11: 353-63,

Greenhalgh R. (1990). "Prognosis of abdominal aortic anrueysm." BMJ; 301: 136-44.

Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG; EVAR trial participants. (2004). "Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial." Lancet; 364: 843–8.

Grimshaw G, Hame. J T, J r (1994). "Prevalence of abdominal aortic aneurysm associated with hypertension in an urban population." J Med Screen; 1: 226-8.

Halak M, Goodman MA, Baker SR. (2006). "The fate of target visceral vessels after fenestrated endovascular aortic repair e general considerations and mid-term results." Eur J Vasc Endovasc Surg; 32: 124-8.

Hammond, E. C. and Garfinke.L (1969). "Coronary Heart Disease, Stroke, and Aortic Aneurysm - Factors in Etiology." Arch Envir Health 19(2): 167-75.

Harris K A, Ameli F M, Lally M, Provan JL, Johnston KW, Goldberg MR, Walker PM. (1986). "Abdominal aortic aneurysm resection in patients more than 80 years old." Surg, Gyne & Obs; 162(6): 536-8.

Harris PL, Buth J, Mialhe C, Myhre HO, Norgren L. (1997). "The need for clinical trials of endovascular abdominal aortic aneurysm stent-graft repair: the EUROSTAR Project. EUROpean collaborators on Stent-graft Techniques for abdominal aortic Aneurysm Repair". J Endovasc Surg; 4: 72–7.

Harris, P.L., Vallabheneni S.R., Desgranges P., Becquemin J.P., Van Marriewijk C., Laheij R.J. (2000). "Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: the EUROSTAR experience." J. Vasc. Surg; 32; 739-49.

Heller JA, Weinberg A, Arons R, Krishnasastry KV, Lyon RT, Deitch JS, Schulick AH, Bush HL Jr, Kent KC. (2000). "Two decades of aortic abdominal aneurysm repair: have we made any progress?", J Vasc Surg; 32:. 1091–100.

Hiramoto JS, Reilly LM, Schneider DB, Sivamurthy N, Rapp JH, Chuter TA (2007): "Long-term outcome and reintervention after endovascular abdominal aortic aneurysm repair using the Zenith stent graft." J Vasc Surg 45:461-465.

Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WR, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM Jr, White CJ, White J, White RA, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Hunt SA, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B. (2006); "ACC/AHA Guidelines for the Management of Patients with Peripheral Arterial Disease (lower extremity, renal, mesenteric, and abdominal aortic" J Vasc Interv Radiol; 17(9): 1383-97

Hobo R, Bath J, EUROSTAR collaborators. (2006). "Secondary interventions following EVAR using current endografts. A EUROSTAR report." J Vasc Surg; 43: 896–902

Holdsworth J. (1994). "Screening for abdominal aortic aneurysm in Northumberland." Br J Surg . 81: 710–2.

Hollier L.H, Reigel M.M, Kazmier F.J, Pairolero P.C, Cherry K.J and Hallett Jr JW. (1986). "Conventional repair of abdominal aortic aneurysm in the high risk patient: a plea for abandonment of non-resective treatment", J Vasc Surg; 3: 712-7.

Hölzenbein TJ, Kretschmer G, Thurnher S, Schoder M, Aslim E, Lammer J, Polterauer P. (2001). "Midterm durability of abdominal aortic aneurysm endograft repair: a word of caution". J Vasc Surg; 33 (2suppl): S46–54.

Hovsepian DM, Hein AN, Pilgram TK, Cohen DT, Kim HS, Sanchez LA, Rubin BG, Picus D, Sicard GA. (2001). "Endovascular abdominal aortic aneurysm repair in 144 patients: correlation of aneurysm size, proximal aortic neck length, and procedure related complications." J Vasc Interv Radiol; 12: 1373-82.

http://www.nice.org.uk

Ingoldby CJ, Wujanto R, Mitchell JE. (1986). "Impact of Vascular Surgery on Community Mortality from Ruptured Aortic Aneurysms." Br J Surg; 73(7): 551-3.

Jaunoo S. (2008). "Endovascular aneurysm repair (EVAR)", Int J Surg; 6(3):266-9

Jean-Claude JM, Reilly LM, Stoney RJ, Messina LM. (1999). "Pararenal aortic aneurysms: the future of open aortic aneurysm repair". J Vasc Surg; 29: 902–12.

Johansen K., Kohler T.R, Nicholls S.C,.Zierler R.E, Clowes A.W and Kazmers A. (1991). "Ruptured abdominal aortic aneurysms: the Harbour view experience", J Vasc Surg; 13 pp. 240–7

Johansson G, Swedenborg J. (1986). "Ruptured abdominal aortic aneurysms: a study of incidence and mortality." Br J Surg 73: 101-3.

Joseph M G, Langsfeld M A, Lusby RJ. (1989). "Infrarenal aortic aneurysm: unusual cause of paraparesis." The Australian And New Zealand J Surg; 59(9): 743-4.

Kent KC, Zwolak RM, Egorova NN, Riles TS, Manganaro A, Moskowitz AJ, Gelijns AC, Greco G (2010). "Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals." J Vasc Surg: 2010 Jul 12: Available online 13 July

Kita Y, Shimizu M, Sugihara N, Shimizu K, Miura M, Koizumi J, Mabuchi H, Takeda R. (1993). "Abdominal Aortic-Aneurysms in Familial Hypercholesterolemia – Case Reports." Angiology; 44(6): 491-9.

Kniemeyer HW, Kessler T, Reber PU, Ris HB, Hakki H, Widmer MK. (2000). "Treatment of ruptured abdominal aortic aneurysm, a permanent challenge or a waste of resources? Prediction of outcome using a multi-organ-dysfunction score." Eur J of Vasc and Endovasc Surg; 19(2): 190-6.

Knott AW, Kalra M, Duncan AA, Reed NR, Bower TC, Hoskin TL, et al. (2008). "Open repair of juxtarenal aortic aneurysms (JAA) remains a safe option in the era of fenestrated endografts". J Vasc Surg; 47(4): 695-701.

Koskas F, and Kieffer E. (1997). "Long-erm survival after elective repaire of infrarenal abdominal aortic aneurysm: results of a prospective multicentric study. association for Academic Research in Vascular Surgery (AURC)." Ann vasc Surg; 11(5):473-81

Kristmundsson T, Sonesson B, Malina M, Björses K, Dias N and Resch T. (2009). "Fenestrated endovascular repair for juxtarenal aortic pathology." J Vasc Surg; 49(3) 568-74

Kudo FA, Nishibe T, Miyazaki K, Murashita T, Yasuda K, Ando M, et al. (2004). "Postoperative renal function after elective abdominal aortic aneurysm repair requiring suprarenal aortic crossclamping." Surg Today; 34: 1010-3.

Lambert A.W, Williams D.J, Budd and J.S, Horrocks M. (1999). "Experimental assessment of proximal stent-graft (intervascular) fixation in human cadaveric infrarenal aortas" Eur J Vasc and Endovasc Surg; 17: (1) 60–5.

LaRoy L L, Cormier P J, Matalon TA, Patel SK, Turner DA, Silver B. (1989). "Imaging of abdominal aortic aneurysms." AJR;152(4): 785-92.

Leather R P, Shah D M, Kaufman JL, Fitzgerald KM, Chang BB, Feustel PJ. (1989). "Comparative-Analysis of Retroperitoneal and Transperitoneal Aortic Replacement for Aneurysm." Surg Gyne & Obs;168(5): 387-93.

Lederle FA, Johnson GR, Wilson SE, Littooy FN, Krupski WC, Bandyk D, Acher CW, Chute EP, Hye RJ, Gordon IL, Freischlag J, Averbook AW, Makaroun MS. (2000). "Yield of repeated screening for abdominal aortic aneurysm after a 4-year interval." Arch Inter Med; 160(8): 1117-21.

Lederle FA, Wilson SE, Johnson GR, Reinke DB, Littooy FN, Acher CW, Ballard DJ, Messina LM, Gordon IL, Chute EP, Krupski WC, Busuttil SJ, Barone GW, Sparks S, Graham LM, Rapp JH, Makaroun MS, Moneta GL, Cambria RA, Makhoul RG, Eton D, Ansel HJ, Freischlag JA, Bandyk D; Aneurysm Detection and

Management Veterans Affairs Cooperative Study Group. (2002). "Immediate repair compared with surveillance of small abdominal aortic aneurysms." New Eng J Med; 346(19): 1437-44.

Leurs LJ, Laheij RJ, Buth J. (2005). "What determines and are the consequences of surveillance intensity after endovascular abdominal aortic aneurysm repair?" Ann Vasc Surg; 19(6): 868-75.

Leurs LJ, Stultiens G, Kievit J, Buth J. (2005). "Adverse events at the aneurysmal neck identified at follow-up after endovascular abdominal aortic aneurysm repair: how do they correlate?." Vascular; 13(5): 261-7.

Lezzi, R., and A. R. Cotroneo. Endovascular repair of abdominal aortic aneurysms: CTA evaluation of contraindications. Abdom. Imaging 31:722–731, 2006.

Li, Z., Kleinstreuer, C. "Analysis of biomechanical factors affecting stent-graft migration in an abdominal aortic aneurysm model." J. Biomechanics, 2006, 39, 2264-73.

Lifeline Registry (2001): "Collaborative evaluation of endovascular aneurysm repair." J Vasc Surg; 34:1139-46,

Liffman K., Lawrence-Brown MM, Semmens JB. Bui A, Rudman M, Hartley DE. (2001). "Analytical modeling and numerical simulation of forces in an endoluminal graft." J Endovasc The; 8: 358–71.

Lindholt JS, Henneberg EW, Fasting H, Juul S. (1996). "Hospital based screening of 65-73 year old men for abdominal aortic aneurysms in the county of Viborg, Denmark." J Med Screen; 3: 43-6.

Lindholt JS, NA Klitgaard B. J, Henneberg E W (2003). "Systemic levels of cotinine and elastase, but not pulmonary function, are associated with the progression of small abdominal aortic aneurysms." Eur J Vasc Endovasc Surg; 26: 418-22.

Louwrens H D, Adamson J, Powell JT, Greenhalgh RM. (1993). "Risk-Factors for Atherosclerosis in Men with Stenosing or Aneurysmal Disease of the Abdominal-Aorta." Inter Angiology 12(1): 21-4.

Lucarotti M, Shaw E, Poskitt K, Heather B. (1993). "The Gloucestershire Aneurysm Screening-Program - the 1st 2 Years Experience." Eur J Vasc Surg; 7(4): 397-401.

Luis R, Leon Jr, Joseph L and Mills Sr. (2010) "Diagnosis and Management of Aortic Mycotic Aneurysms" Vasc Endovasc Surg; 44; 5-13

Lumsden AB., Allen RC., Chaikof EL, Resnikoff M, Moritz MW, Gerhard H, Castronuovo JJ Jr. (1995). "Delayed rupture of aortic aneurysms following endovascular stent grafting." Am J Surg; 170: 174–8.

Lyratzopoulos G, Walker N, Varty K, Campbell WB Winterborn RJ, Amin I. (2009). "Preferences for endovascular (EVAR) or open surgical repair among patients with abdominal aortic aneurysms under surveillance." J Vasc Surg; 49(3): 576-81

M. Malina, B. Lindblad, K. Ivancev, M. Lindh, J. Malina and J. Brunkwall. (1998). "Endovascular AAA exclusion: will stents with hooks and barbs prevent stent-graft migration?" J Endovasc Surg; 5:(4) pp. 310–17.

Macsweeney ST, Ellis M, Worrell PC, Greenhalgh RM, Powell JT. (1994). "Smoking and Growth-Rate of Small Abdominal Aortic-Aneurysms." Lancet; 344(8923): 651-2.

Macsweeney ST, Omeara M, Alexander C, O'Malley MK, Powell JT, Greenhalgh RM. (1993). "High Prevalence of Unsuspected Abdominal Aortic-Aneurysm in Patients with Confirmed Symptomatic Peripheral or Cerebral Arterial-Disease." Bri J of Surg; 80(5): 582-4.

MacSweeney ST, Powell JT, Greenhalgh RM. (1994). "Pathogenesis of abdominal aortic aneurysm." Bri J Surg; 81(7): 935-41.

Majumder PP, Stjean PL, Ferrell RE, Webster MW, Steed DL. (1991). "On the Inheritance of Abdominal Aortic Aneurysm." Ameri J Human Genetics 48(1): 164-70.

Manning M W, Cassis L A, Daugherty A. (2003). "Differential effects of doxycycline, a broad-spectrum matrix metalloproteinase inhibitor, on angiotensin II-induced atherosclerosis and abdominal aortic aneurysms." Arteriosc Thromb and Vasc Bio; 23(3): 483-8.

Marc L. Schermerhorn, A. James O'Malley, Ami Jhaveri, Philip Cotterill, Frank Pomposelli and Bruce E. Landon. (2008). "Endovascular vs. Open Repair of Abdominal Aortic Aneurysms in the Medicare Population". N Engl J Med; 358: 464-74.

van Marrewijk C, Buth J, Harris PL, Norgren L, Nevelsteen A, Wyatt MG. (2002). "Significance of endoleaks after endovascular repair of abdominal aortic aneurysms: The EUROSTAR experience" J. Vasc. Surg.;35:461-73.

Matsumura J.S., Moore W.S. (1998). "Clinical consequences of periprosthetic leak after endovascular repair of abdominal aortic aneurysm." J Vasc Surg.;27:606–13.

May J, White GH, Waugh R, Ly CN, Stephen MS, Jones MA, Harris JP. (2001). "Improved survival after endoluminal repair with second-generation prostheses compared with open repair in the treatment of abdominal aortic aneurysms: a 5-year concurrent comparison using life table method." J Vasc Surg; 33 (2 suppl) : S21–6.

McFarlane M J (1991). "The Epidemiologic Necropsy for Abdominal Aortic-Aneurysm." Jama; 265(16): 2085-8.

Mealy K A S.(1988). "The true incidence of ruptured abdominal aortic aneurysms." Eur J of Vasc; 2: 405-8.

Melton LJ, Bickerstaff LK, Hollier LH, Van Peenen HJ, Lie JT, Pairolero PC, Cherry KJ, O'Fallon WM. (1984). "Changing Incidence of Abdominal Aortic-Aneurysms - a Population Based Study." Am J Epid 120(3): 379-86.

Miralles M W, Sicard W, Thompson G.A, Reilly R J.M. (1999). "Indomethacin inhibits wxpansion of wxperimental aortic aneurysms via inhibition of the cox2 isoform of cyclooxygenase." J Vasc Surg; 29: 884-92.

Miralles M, Wester W, Sicard GA, Thompson R, Reilly JM. (1999). "Indomethacin inhibits expansion of experimental aortic aneurysms via inhibition of the cox2 isoform of cyclooxygenase." J of Vasc Surg 29(5): 884-92.

Mohan I.V., Laheij R.J. and Harris P.L. (2001)." Risk factors for endoleak and the evidence for stent-graft oversizing in patients undergoing endovascular aneurysm repair" Eur J Vasc and Endovasc Surg; 21: (4) pp. 344–9.

Mohan IV, Harris PL, van Marrewijk CJ, Laheij RJ, How TV. (2002). "Factors and forces influencing stent-graft migration after endovascular aortic aneurysm repair." J Endovasc Ther; 9: 748–55.

Moher D, Cole C W, Hill GB. (1992). "Epidemiology of Abdominal Aortic-Aneurysm - the Effect of Differing Definitions." Eur J Vasc Surg 6(6): 647-50.

Moritz JD, Rotermund S, Keating DP, Oestmann JW. (1996). "Infrarenal abdominal aortic aneurysms: implications of CT evaluation of size and configuration for placement of endovascular aortic grafts". Radiology; 198: 463-6.

Morris GE, Hubbard CS, Quick CR. (1994). "An Abdominal Aortic-Aneurysm Screening-Program for All Males over the Age of 50 Years." Eur J Vasc Surg; 8(2): 156-60.

Morris L, Delassus P, Walsh M, McGloughlin T.. (2004). "A mathematical model to predict the in vivo pulsatile drag forces acting on bifurcated stent grafts used in endovascular treatment of abdominal aortic aneurysms (AAA)." J Biomech; 37: 1087–95.

Morrisey NJ, Faries PL, Teoderescu V, Hollier L, Marin ML. (2002). "Transrenal bare stents in endovascular treatment of abdominal aortic aneurysms." J Invasive Cardiol; 14: 36-40.

Muhs BE, Verhoeven EL, Zeebregts CJ, Tielliu IF, Prins TR, Verhagen HJM, et al. (2006). "Mid-term results of endovascular aneurysm repair with branched and fenestrated endografts." J Vasc Surg; 44: 9-15

Nevelsteen A, Maleux G. (2004)." Endovascular abdominal aortic aneurysm treatment: device-specific outcomes". J Cardiovasc Surg; 45: 307–19.

Noel A.A, Gloviczki P, Cherry Jr K.J, Bower T.C, Panneton J.M and. Mozes G.I et al. (2001). "Ruptured abdominal aortic aneurysms: the excessive mortality rate of conventional repair", J Vasc Surg; 34. 41–6.

Nonami Y, Ogoshi S (1996). "Chronic contained rupture of abdominal aortic aneurysms." J Cardiovasc Surg; (Torino) 37: 252–8.

Nordon I.M, Hinchliffe R.J, Holt P.J, Loftus I.M, Thompson M.M. (2009). "Modern Treatment of Juxtarenal Abdominal Aortic Aneurysms with Fenestrated

Endografting and Open Repair - A Systematic Review" Eur J Vasc Endovasc Surg; 38, 35-41

Norgard O, K Angquist O R. (1984). "Familial occurrence of abdominal aortic aneurysms." Surgery; 95: 589-91.

Norman PE, Castleden WM, Hockey RL. (1991). "Prevalence of Abdominal Aortic-Aneurysm in Western Australia." Br J Surg; 78(9): 1118-21.

O Norgard , O. R., K Angquist, (1984). "Familial occurrence of abdominal aortic aneurysms." Surgery; 95: 589-91.

O'Neill S, Greenberg RK, Haddad F, Resch T, Sereika J, Katz E. A. (2006). "prospective analysis of fenestrated endovascular grafting: intermediateterm Outcomes". Eur J Vasc Endovasc Surg; 32, 2; 115-23.

Ockert S, Schumacher H, Bockler D, Malcherek K, Hansmann J, Allenberg J. (2007). "Comparative early and midterm results of open juxtarenal and infrarenal aneurysm repair." Langenbecks Arch Surg; 392: 725-30.

Ogren M, Bengtsson H, Bergqvist D, Ekberg O, Hedblad B, Janzon L. (1996). "Prognosis in elderly men with screening-detected abdominal aortic aneurysm." Eur J Vasc and Endovasc Surg; 11(1): 42-7.

Orr WM and Davies M. (1974). "Simplified repair of abdominal aortic aneurysms using non-bifurcated (straight) inlay prosthesis." Br J Surg;. 61(10): 847-9.

Osler, W. (1905). "Aneurysm fo the abdominal aorta." Lancet; 2: 1089.

Park JH, Chung JW, Choo IW, Kim SJ, Lee JY, Han MC. (1996). "Fenestrated stent-grafts for preserving visceral arterial branches in the treatment of abdominal aortic aneurysms: preliminary experience" J Vasc Interv Radiol; 7: 819-23.

Parodi JC, Palmaz JC, Barone H,D. (1991) "transfemoral intraluminal graft implantation for abdominal aortic aneurysms." Ann Vasc Surg 5(6): 491-9

Pearce JD, Edwards MS, Stafford JM, Deonanan JK, Davis RP, Corriere MA, et al. (2007). "Open repair of aortic aneurysms involving the renal vessels." Ann Vasc Surg; 21(6): 676-86.

Petrik PV, Moore WS, "Endoleaks following endovascular repair of abdominal aortic aneurysm: the predictive value of preoperative anatomic factors – a review of 100 cases." J Vasc Surg 33 (4) (2001), p. 739–44.

Pfammatter T, Lachat ML, Kunzli A, Baur DR, Koppensteiner R, Turina M, Blum U. (2002). "Short-term results of endovascular AAA repair with the Excluder bifurcated stent-graft." J Endovasc Ther; 9: 474–80.

Pleumeekers H, Hoes A W, van der Does E, van Urk H, Hofman A, de Jong PT, Grobbee DE. (1995). "Aneurysms of the abdominal aorta in older adults - The Rotterdam study." Amer J of Epidemi 142(12): 1291-99.

Pleumeekers H, Hoes A. W, van der Does E, van Urk H, Grobbee DE. (1994). "Epidemiology of Abdominal Aortic-Aneurysms." Eur J Vasc Surg 8(2): 119-28.

Pleumeekers H, Hoes A. W, van der Does E, van Urk H, Hofman A, de Jong PT, Grobbee DE. (1995). "Aneurysms of the abdominal aorta in older adults - The Rotterdam study." Am J Epid 142(12): 1291-99.

Politz J.K., Newman V.S., Stewart M.T. (2000). "Late abdominal aortic aneurysm rupture after AneuRx repair: a report of three cases." J Vasc Surg; 31: 599–606.

Powell, J T; Brown, Louise C; Greenhalgh, Roger; Thompson M, Simon G; EVAR Trial Participants (2008).. "The Rupture Rate of Large Abdominal Aortic Aneurysms: Is This Modified by Anatomical Suitability For Endovascular Repair?" Ann Surg; 247(1), 173-9

Prince MR, Narasimham DL, Stanley JC, Wakefield TW, Messina LM, Zelenock GB, Jacoby WT, Marx MV, Williams DM, Cho KJ. (1995). "Gadolinium-enhanced magnetic resonance angiography of abdominal aortic aneurysms." J Vasc Surg: 21(4): 656-69.

Prinssen M, Verhoeven EL, Buth J et al. Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group (2004), "A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms". N Eng J Med; 351: 1607–18

Rasmussen TE, Hallett JW, Schutte S, Harmsen WS, O'Fallon WM and.Weyand CM (2001), "Genetic similarity in inflammatory and degenerative abdominal aortic aneurysms: a study of human leukocyte antigen class II disease risk genes", J Vasc Surg **34** pp. 84–89

Rasmussen T E. and Hallett J W, Jr (1997). "Inflammatory aortic aneurysms. A clinical review with new perspectives in pathogenesis." Ann Surg; 225(2): 155-64.

Reed D, Reed C, Stemmermann G, Hayashi T. (1992). "Are Aortic-Aneurysms Caused by Atherosclerosis." Circulation; 85(1): 205-11.

Reilly J M And Tilson M. D. (1989). "Incidence and etiology of abdominal aortic aneurysms." The Surg Clinics N Ameri 69(4): 705-11.

Resch T, Malina M, Lindblad B, Malina J, Brunkwall J, Ivancev K. (2000). "The impact of stent design on proximal stent-graft fixation inthe abdominal aorta: an experimental study". Eur J Vasc Endovasc Surg; 20(2): 190-5.

Resch, T., Ivancev, K., Brunkwall, J., Nyman, U., Malina, M., Lindblad, B. (1999). "Distal migration of stent-grafts after endovascular repair of abdominal aortic aneurysms." J. Vasc. Interven. Radiol., 10, 257-64.

Rose AG and Dent DM(1981), "Inflammatory variant of abdominal aortic atherosclerotic aneurysm." Arch Pathol Lab Med **105** pp. 409–413

Rutherford, RB., and Krupski WC. "Current status of open versus endovascular stent-graft repair of abdominal aortic aneurysm." J. Vasc. Surg. 39:1129–1139, 2004

Ryan SV, Calligaro KD, McAffee-Bennett S, Doerr KJ, Chang J, Dougherty MJ. (2004). "Management of juxtarenal aortic aneurysms and occlusive disease with

preferential suprarenal clamping via a midline transperitoneal incision: technique and results." Vasc Endovasc Surg; 38 (5): 417-22.

Sackett D L H, Guyatt G.H. and Tugwell, P. (1991). "Clinical epidemiology: a basic science for clinical medicine". Boston, Little, Brown and Company: 69–152.

Sampaio S.M.,. Panneton J.M, Mozes G., Andrews J.C, Noel A.A and Kalra M. Bower TC, Cherry KJ, Sullivan TM, Gloviczki P. (2005). "AneuRx device migration: incidence, risk factors, and consequences" Ann Vasc Surg; 19: (2) pp. 178–85.

Sampaio SM,. Panneton JM, Mozes GI. (2004). "Proximal Type I Endoleak After Endovascular Abdominal Aortic Aneurysm Repair: Predictive Factors." Ann of Vasc Surg 18; 6; 621-8

Sarac TP, Clair DG, Hertzer NR, Greenberg RK, Krajewski LP, O'Hara PJ, Ouriel K. (2002). "Contemporary results of juxtarenal aneurysm repair." J Vasc Surg; 36 (6): 1104-11.

Schlosser F.J., Gusberg R.J, Dardik A, Lin P.H, Verhagen H.J and Moll F.L. Muhs BE. (2009). "Aneurysm rupture after EVAR: can the ultimate failure be predicted?" European Journal of Vascular and Endovascular Surgery 37 (1) 15–22.

Schurink G.W, Aarts N.J, Van Baalen J.M, Schultze Kool L.J and Van Bockel J.H, Stent attachment site-related endoleakage after stent graft treatment: an in vitro study of the effects of graft size, stent type, and atherosclerotic wall changes, Journal of Vascular Surgery 30 (4) (1999), pp. 658–67.

Scott RA, Wilson NM, Ashton HA, Kay DN. (1995). "Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5 year results of a rendomised controlled study." Br J Surg; 82: 1066-70.

Scott RA, Ashton HA, Kay DN. (1991). "Abdominal Aortic-Aneurysm in 4237 Screened Patients - Prevalence, Development and Management over 6 Years." Br J Surg 78; (9): 1122-5.

Scurr JRH, Brennan JA, Gilling-Smith GL, Harris PL, Vallabhaneni SR, McWilliams RG. (2008). "Fenestrated endovascular repair for juxtarenal aortic aneurysm". Br J Surg 95: 326-32

Semmens JB, Lawrence-Brown M, Hartley D, Allen YB, Green R, Nadkarni S. (2006). "Outcomes of fenestrated endografts in the treatment of abdominal aortic aneurysm in Western Australia." J Endovasc Ther 13: 320-9.

Sho E, Sho M, Hoshina K, Kimura H, Nakahashi TK, Dalman RL. (2003). "Hemodynamic forces modulate murine AAA progression." American Association of Vascular Surgeons Annual Meeting, Chicago, IL.

Shortell CK, Johansson M, Green RM, Illig KA. (2003). "Optimal operative strategies in repair of juxtarenal abdominal aortic aneurysms." Ann Vasc Surg; 17: 60-5.

Sicard GA, Reilly JM, Rubin BG, Thompson RW, Allen BT, Flye MW, Schechtman KB, Young-Beyer P, Weiss C, Anderson CB. (1995). "Transabdominal Versus

Retroperitoneal Incision for Abdominal Aortic-Surgery - Report of a Prospective Randomized Trial." J Vasc Surg; 21(2): 174-83.

Simon G, Nordgren D, Connelly S, Shultz PJ. (1996). "Screening for abdominal aortic aneurysms in a hypertensive patient population." Arch Inter Med; 156(18): 2081-84.

Smith FC, Grimshaw GM, Paterson IS, Shearman CP, Hamer JD. (1993). "Ultrasonographic Screening for Abdominal Aortic-Aneurysm in an Urban Community." Br J Surg; 80(11): 1406-09.

Stanley BM, Semmens JB, Mai Q, Goodman MA, Hartley DE, Wilkinson C (2001) et al. "Evaluation of patient selection guidelines for endoluminal AAA repair with the Zenith Stent-Graft: the Australasian experience". J Endovasc Ther; 8:457-64.

Sternbergh III WC, Money SR, Greenberg RK and Chuter TA. (2004). "Influence of endograft oversizing on device migration, endoleak, aneurysm shrinkage, and aortic neck dilation: results from the Zenith multicenter trial." J Vasc Surg 39 (1), pp. 20–6

Sternbergh WC, Carter G, York JW, Yoselevitz M, Money SR. (2002). " Aortic neck angulation predicts adverse outcome with endovascular abdominal aortic aneurysm repair." J Vasc Surg.;35:482–6.

Sterpetti AV, Hunter WJ,. Feldhaus RJ, Chasan P, McNamara BS., Cisternino S. and Schultz RD (1989). "Inflammatory aneurysms of the abdominal aorta: incidence, pathologic and etiologic considerations" J Vasc Surg :9: 643–650.

Strachan D. P. (1991). "Predictors of Death from Aortic-Aneurysm among Middle-Aged Men - the Whitehall Study." Br J Surg 78(4): 401-4.

Sutalo, I.D., Liffman, K., Lawrence-Brown, M.M.D., Semmens, JB, (2005). Experimental force measurements on a bifurcated endoluminal stent graft model: Comparison with theory. Vascular, 13, 98-106.

Suzuka I K A. (1966). "Binding of specfic sRNA to 30S ribosomal subunits: effects of 50S ribosomal subunits." Proc Natl Acad Sci; 55: 1483-6.

SVS/NAISCVS. (1991). "Suggested standards for reporting on arterial aneurysms." J Vasc Surg; 13: 452-8.

Thomas SM, Gaines PA, Beard JD. Vascular surgical society of Great Britain and Ireland (1999) "RETA: the registry of endovascular treatment of abdominal aortic aneurysms." Br J Surg 86:711-19.

Thomas PRS, Stewart R D (1988). "Abdominal Aortic-Aneurysm." British Journal of Surgery; 75(8): 733-6.

Thompson JP, Boyle JR, Thompson MM Strupish J, Bell PR, Smith G. (1999). "Cardiovascular and catecholamine responses during endovascular and

conventional abdominal aortic aneurysm repair." Eur J Vasc Endovasc Surg; 17: 326–33

Thompson M M S, Jacobs R.D, Jonathan P G and D Beard. (2001). "Arterial aneurysms". Vasc and Endovasc Surg; W.B. Saunders: 241-66.

Thompson MM, Nasim A, Sayers RD, Thompson J, Smith G, Lunec J, Bell PR. (1996). "Oxygen free radical and cytokine generation during endovascular and conventional aneurysm repair". Eur J Vasc Endovasc Surg 12:70–5.

Thompson, M. M, Jacobs,M.J. H. M. (2001). "Arterial aneurysms". Vascular and Endovascular Surgery;. P. G. Jonathan D Beard, W.B. Saunders: 241-66.

Tilson M D and Seashore M. R (1984). "Fifty families with abdominal aortic aneurysms in two or more first-order relatives." The Am J Surg; 147(4): 551-53.

Tilson, M. D. and Seashore M. R (1984). "Human genetics of the abdominal aortic aneurysm." Surg. Gyne. Obst;. 158(2): 129-32.

Tonnessen BH, Sternbergh III WC, Money SR. (2005). "Mid- and long-term device migration after endovascular abdominal aortic aneurysm repair: a comparison of AneuRx and Zenith endografts". J Vasc Surg; 42(3): 392-400.

Torsello, G.B., Klenk, E.,. Kasprzak, B., Umscheid, T. (1998). "Rupture of abdominal aortic aneurysm previously treated by endovascular stent graft." J Vasc Surg., 28, 184–87.

Treharne G D, Goodall J R, Loftus S, Bell P R and Thompsom,M.M. (1999). "Marimastat inhibits elastin degradation and matrix metalloproteinase 2 activity in a model of aneurysm disease." Br J Surg; 86: 1053-58.

Trial Participants, T. U. S. A. (1998). "Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms." The Lancet; 352(9141): 1649-55.

Vallabhaneni, SR, Harris, PL. (2001). "Lessons learnt from the EUROSTAR registry on endovascular repair of abdominal aortic aneurysm." Eur. J. Radiol; 39: 34-41

van Herwaarden JA, van de Pavoordt ED, Waasdorp EJ, Albert VJ, Overtoom TT, Kelder JC, Moll FL, de Vries JP. (2007). "Long-term singlecenter results with AneuRx endografts for endovascular abdominal aortic aneurysm repair". J Endovasc Ther; 14(3): 307-17.

van Marrewijk C, Buth J, Harris PL, Norgren L, Nevelsteen A, Wyatt MG (2002). "Significance of endoleaks after endovascular repair of abdominal aortic aneurysms: The EUROSTAR experience". J Vase Surg; 35: 461-73

van Marrewijk CJ, Leurs LJ, Vallabhaneni SR, Harris PL, Buth J,Laheij RJ. (2005). "Risk-adjusted outcome analysis of endovascular abdominal aortic aneurysm repair in a large population: how do stent-grafts compare?" J Endovasc Ther; 12(4): 417-29.

van Prehna J, Schlösserb, Muhs BE, Verhagenc H.J.M, Moll FL and. van Herwaardena J.A. (2009). "Oversizing of Aortic Stent Grafts for Abdominal

Aneurysm Repair: A Systematic Review of the Benefits and Risks." Eur J Vasc and Endovasc Surg; 38 (1); 42-53

Vander Vliet JA. and Boll APM (1997). "Abdominal aortic aneurysm." Lancet; 349(9055): 863-6.

Veerapen R, Dorandeu A, Serre I, Berthet JP, Marty-Ane CH, Mary H, Alric P. (2003). "Improvement in proximal aortic endograft fixation: An experimental study using different stent-grafts in human cadaveric aortas." J. Endovasc. Ther; 10, 1101-09.

Veeraswamy, R. K. T., R.W. (2004). "causation of aortic ameurysms". Charing Cross Synposium, London, BIBA Publishing.

Veith FJ, Baum RA, Ohki T, Amor M, Adiseshiah M, Blankensteijn JD (2002)et al. "Nature and significance of endoleaks and endotension: summary of opinions expressed at an international conference". J Vase Surg; 35: 1029-35;

Veith FJ, Parodi J.A, and Marin M (1999). "History potential influence and facility requirements of transluminally placed endovascular grafts". Endovascular grafting techniques; Editors, William and Wilkins, Philadelphia pp. 1–5.

Verhoeven EL, Prins TR, Tielliu IF. van den Dungen JJ, Zeebregts CJ, Hulsebos RG, van Andringa de Kempenaer MG, Oudkerk M, van Schilfgaarde R. (2004). "Treatment of short-necked infrarenal aortic aneurysms with fenestrated stent-grafts: short-term results." Eur J Vasc Endovasc Surg.;27:477–83.

Verloes A, Koulischer N S and Limet R. (1995). "Aneurysms of the abdominal aorta: familial and genetic aspects in three hundred thirteen pedigrees." J Vasc Surg 21: 646–655.

Volodos NL, Karpovich IP, Troyan VI. Kalashnikova Yu, Shekhanin VE, Ternyuk NE. Neoneta AS. Ustinov NI. Yakovenko LF. (1991). "Clinical experience in the use of self-fixing synthetic prostheses for remote endoprosthetics of the thoracic and the abdominal aorta and iliac arteries through the femoral artery and as intraoperative endoprosthesis for aorta reconstruction." Vasa Suppl; 33: 93-5.

Volodos, S. M, Sayers, R. D., Gostelow, J. P., Bell P. (2003). "Factors Affecting the Displacement Force Exerted on a Stent Graft after AAA Repair—An In vitro Study." Eur J Vasc Endovasc Surg; 26, 596–601.

Waasdorp E. de Vries J.P.M. Sterkenburg A., Vos J.-A, Kelder H.J.C, Moll F.L, Zarins C.K. (2009). "The Association between Iliac Fixation and Proximal Stent-graft Migration during EVAR Follow-up:Mid-term Results of 154 Talent Devices" Eur J Vasc Endovasc Surg 37, 681-7

Waasdorp EJ, de Vries JP, Hobo R, Leurs LJ, Buth J, Moll FL. (2004). "Aneurysm diameter and proximal aortic neck diameter influence clinical outcome of endovascular abdominal aortic repair: a 4-year EUROSTAR experience." Ann Vasc Surg; 19(6): 755-61.

West CA, Noel AA, Bower TC, Cherry Jr KJ, Gloviczki P, Sullivan TM, Kalra M, Hoskin TL, Harrington JR. (2006). "Factors affecting outcomes of open surgical repair of pararenal aortic aneurysms: a 10-year experience." J Vasc Surg; 43(5): 921-7.

White GH, Yu W, May J, Chaufour X, Stephen MS. (1997). "Endoleak as a complication of endoluminal grafting of abdominal aortic aneurysms: classification, incidence, diagnosis and management." J Endovasc Surg; 4: 152-68

White GH, Yu W, May J. (1996). ""Endoleak": a proposed new terminology to describe incomplete aneurysm exclusion by an endoluminal graft." J Endovasc Surg; 3: 124-5.)

Williams, P. L. W., R. Dyson, M. and Bannister,L.H. (1989). Angiology. Gray's anatomy;. L. H. Bannister. Edinburgh, Churchill Livingstone: 662–58.

Wilmink, A. B. M. and Quick C. R. G. (1998). "Epidemiology and potential for prevention of abdominal aortic aneurysm." Br J Surg; 85(2): 155-62.

Wilt TJ, Lederle FA, Macdonald R, Jonk YC, Rector TS, Kane RL (2006). Comparison of endovascular and open surgical repairs for abdominal aortic aneurysm. Evid Rep Technol Assess;144: 1-113.

Wolf YG, Hill BR, Lee WA, Corcoran CM, Fogarty TJ, Zarins CK. (2002). "Eccentric stent graft compression: an indicator of insecure proximal fixation of aortic stent graft." J Vasc Surg; 33: 481–7.

Wong J G (2000). "Appropriate abdominal aortic aneurysm screening." Postgrad Med; 107(3): 21-2.

Woodburn K.R, Chant H, Davies J.N, Blanshard K.S and.Travis S.J. (2001). "Suitability for endovascular aneurysm repair in an unselected population", Br J Surg 88 pp. 77–81.

Wyffels P, Dolmath B and Blum U. (2000). "Abdominal aortic aneurysms: natural history and surgical treatment." In current clinical practice; pp. 43–54.

Yochum L J R, Rowe L.J et al.(1996). "Hematologic and vascular disorders." Essentials of skeletal radiology; Baltimore, Williams & Wilkins: 1243–326.

Yucel, EK. (1994). "MR angiography for evaluation of abdominal aortic aneurysm: has the time come?" Radiology; 192(2): 321-3.

Zarins C K, Hrikkinrn M A Townsend JR C M and Hill B B. (2004). "Aneurysmal Vascular Disease" Sabiston Textbook of Surgery;. . Philadelphia, Elsevier and W B Saunders: 1974-5.

Zarins C K, White R A, Fogarty T J (2000). "Aneurysm rupture after endovascular repair using the AneuRx stent graft." J Vasc Surg; 31: 960–70.

Zarins CK, Bloch DA, Crabtree T, Matsumoto AH, White RA, Fogarty TJ. (2003). "Stent graft migration after endovascular aneurysm repair: importance of proximal fixation". J Vasc Surg; 38(6):1264-72.

Zarins CK, Shaver DM, Arko FR, Schubart PJ, Lengle SJ, Dixon SM. (2002). "Introduction of endovascular aneurysm repair into community practice: initial results with a new Food and Drug Administration-approved device." J Vasc Surg; 36:226–32.

Zarins CK, White RA, Schwarten D, Kinney E, Diethrich EB, Hodgson KJ, Fogarty TJ. (1999). "AneuRx stent graft versus open surgical repair of abdominal aortic aneurysms: multicenter prospective clinical trial." J Vasc Surg; 29: 292–305

Zarins CK. (2003). "AneuRx Clinical Investigation. The US AneuRx Clinical Trial: 6-year clinical update 2002." J Vasc Surg; 37:904 – 8.

Zeebregts CJ, Geelkerken RH, van der Palen J, et al. (2004). "Outcome of abdominal aortic aneurysm repair in the era of endovascular treatment". Br J Surg; 91: 563–8.

Ziegler P, Avgerinos ED, Umscheid T, Perdikides T, Stelter WJ. (2007). "Fenestrated endografting for aortic aneurysm repair: a 7-year experience." J Endovasc Ther; 14: 609-18.

Zipes, W. M. M,. Smith L. H . (1990). Aortic and peripheral vascular disease. Cecil essentials of medicine (ed.). Philadelphia, W. B. Saunders: 114–9.

J ENDOVASC THER
2007;14:168–175

◆ EXPERIMENTAL INVESTIGATION ◆

Comparison of the Fixation Strength of Standard and Fenestrated Stent-Grafts for Endovascular Abdominal Aortic Aneurysm Repair

Samuel S. N. Zhou, MRCS, MRCSEd[1,2]; Thien V. How, PhD[1]; S. Rao Vallabhaneni, MD, FRCS[2]; Geoffrey L. Gilling-Smith, MS, FRCS[2]; John A. Brennan, MD, FRCS[2]; Peter L. Harris, MD, FRCS[2]; and Richard McWilliams, FRCR[3]

[1]Department of Clinical Engineering, University of Liverpool, England, UK. Departments of [2]Vascular Surgery and [3]Radiology, Royal Liverpool University Hospital, Liverpool, England, UK.

Purpose: To determine whether fenestrated stent-grafts provide better stability to resist migration than standard non-fenestrated stent-grafts.

Methods: Truncated fenestrated stent-grafts with a single fenestration were deployed in bovine aortic segments with a side branch. Balloon-expandable stents were then delivered into the branches. Similarly, standard stent-grafts of the same dimensions were deployed for comparison. The aorta was pressurized to achieve stent-graft oversizing of 5%, 10%, or 20%. The force required to cause distal migration was recorded by a digital force gauge attached to the stent-graft.

Results: Displacement of the stent-grafts occurred in 2 distinct phases: an initial yield during which the barbs embedded in the aortic wall and a final displacement leading to significant migration and dislodgement of the device. The displacement force that initiated each phase was dependent upon the degree of oversizing of the stent-graft relative to the aortic diameter. For 5%, 10%, and 20% oversizing, the mean displacement forces in the initial displacement phase were 3.39±0.37, 4.32±0.63, and 7.69±1.18 N, respectively, in non-fenestrated grafts and 10.48±1.23, 11.45±1.48, 12.12±1.42 N in fenestrated grafts. The displacement forces in the final displacement phase were 8.10±0.92, 10.76±1.74, and 16.82±0.92 N for non-fenestrated and 22.56±1.60, 28.24±1.56, and 33.01±1.75 N for fenestrated stent-grafts. The differences in displacement forces between standard and fenestrated stent-grafts were significant for both phases ($p<0.001$) at all oversizing levels.

Conclusion: Improvement in fixation strength was noted with increasing stent-graft oversizing of up to 20%. Fenestrated stent-grafts offer higher ultimate fixation compared to standard devices. However, the ultimate fixation strength was not recruited until an initial phase of short migration occurred as the barbs engaged. While this movement is inconsequential with standard stent-grafts, it has the potential to crush the stents placed into aortic side branches with fenestrated endografts.

J Endovasc Ther 2007;14:168–175

Key words: abdominal aortic aneurysm, endovascular repair, stent-graft, fenestrated stent-graft, bovine aorta, displacement force, migration

The authors have no commercial, proprietary, or financial interest in any products or companies described in this article.

Address for correspondence and reprints: Thien How, Division of Clinical Engineering, School of Clinical Sciences, University of Liverpool, Liverpool L69 3GA, UK. Fax: 44-151-706-5803; E-mail: *thienhow@liv.ac.uk*

Since endovascular abdominal aortic aneurysm (AAA) repair (EVAR) was introduced more than a decade ago, the technique has been widely accepted worldwide. Clinical trials demonstrated short-term survival benefit over open repair of large AAAs.[1,2] Although stent-graft design and EVAR techniques have much improved, the durability of stent-grafts still raises concerns. One of the most important complications affecting the long-term success is stent-graft migration, that is, movement of a fully deployed stent-graft relative to the vascular anatomy, which has the potential to cause attachment-site endoleak and even aneurysm rupture.[1–5] A deployed stent-graft constantly faces physiological forces[6–8] that can initiate migration, and these devices should be designed to resist displacement.

Fenestrated stent-grafts have been introduced to extend the applicability of EVAR to patients with aneurysm necks that are too short to satisfactorily position a conventional stent-graft.[9,10] A fenestrated stent-graft has fabric that extends to a level above one or more visceral arteries. Perfusion of the visceral arteries below the fabric margin is preserved via one or more fenestrations in the stent-graft fabric that are incorporated during manufacture and positioned accurately at the time of deployment. Usually stents are placed through the fenestration into the visceral arteries to provide additional anchorage to the stent-graft, although they are not intended primarily for this purpose.

The aim of this study was to compare the proximal fixation strength of standard and fenestrated stent-grafts in an in vitro bovine aortic model.

METHODS

Experimental Design

The bench top experiment (Fig. 1) comprised a pressurised bovine aorta into which the proximal portion of a standard or fenestrated Zenith stent-graft (Cook Europe, Bjaeverskov, Denmark) was deployed. Force was applied to the stent-graft to make it migrate within the aorta under observation; this displacement force was measured with a calibrated digital force gauge. Since stent-grafts are oversized in relation to the aneurysm neck in routine clinical practice, the experiments were carried out with oversizing of 5%, 10%, and 20% for both types of stent-grafts. For each type of device, 8 experiments were conducted at 5% and 10% oversizing and 6 at 20% oversizing for a total of 22 experiments per device type.

Tissue Preparation

Fresh bovine aortas were obtained from an abattoir. The abdominal portion was retained, and all adherent non-vascular tissue was removed. Small side branches were ligated at ~3 mm from the origin, and larger branches (5–6 mm wide when pressurized) were identified for stenting with the fenestrated grafts. A length of at least 3 cm was provided to accommodate the stent. Any leaking areas were oversewn using 4–0 Vicryl sutures. The aortas were stored in normal saline at 4°C for a maximum of 24 hours after

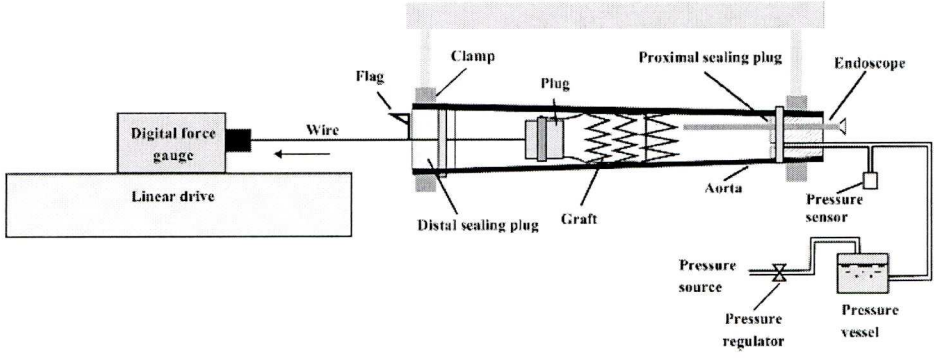

Figure 1 ◆ Diagram of the experimental setup.

preparation, during which the experiments were conducted.

Stent-Graft Oversizing

First, the internal diameter of the pressurized bovine aorta was determined from the relationship of the internal diameter to pressure over the range 0 to 140 mmHg at intervals of 2.5 cm along the length of the aortic segment. The wall thickness at each axial location was measured using digital calipers. The aorta was then plugged at both ends, and the lumen was pressurized with saline at a pressure of 140 mmHg. The length of the aortic segment at this pressure was measured. The ends of the aorta were then securely clamped so that the length of the aorta remained constant during the experiment. The external diameters of the aorta over the range 0 to 140 mmHg pressure were determined at each marked location using the digital calipers. Although the bovine aorta is tapered over its full length, each 2.5-cm segment between the marks was considered to be a straight tube whose diameter was the average of the proximal and distal end diameters of that particular segment. Assuming that the volume of the aortic wall remains constant at any luminal pressure, the internal diameter can be calculated from the external diameter. For a subsegment of length L, proximal external diameter D_p, and distal external diameter D_d, the volume V of the aortic wall is represented by the formula:

$$V = \frac{\pi L}{4}(D_o^2 - D_i^2)$$

Where

$$D_i = \frac{Dp_i + Dd_i}{2}$$

$$D_o = \frac{Dp_o + Dd_o}{2}$$

The subscript o denotes external, and subscript i, the internal dimensions.

Knowing the external diameter D_o, the internal diameter can be calculated as:

$$D_i = \sqrt{D_o^2 - \frac{4V}{\pi L}}$$

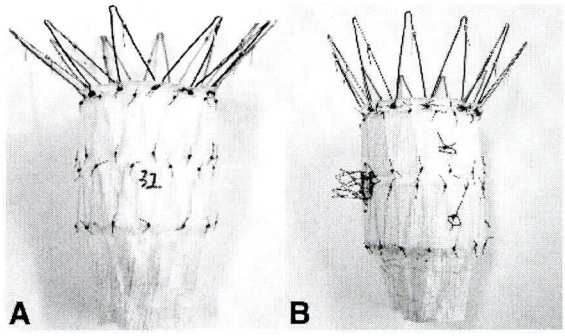

Figure 2 ◆ (A) Standard and **(B)** fenestrated stent-grafts truncated to 53 mm in length.

Once the relationship between the luminal pressure and the internal diameter of the aorta was determined, it was possible to establish the segment in the aorta wherein a stent-graft of a certain diameter should be deployed, as well as the pressure that should be applied to achieve a known oversizing (5%, 10%, or 20% in this study).

Stent-Graft Construction and Deployment

Zenith stent-grafts have a proximal bare stent with fixation barbs located midway along alternate stent struts. This stainless steel stent segment is fixed to the main trunk of the stent-graft with monofilament sutures. Stent-grafts of 28, 30, and 32 mm nominal diameter were deployed within different aortic segments under appropriate pressure to achieve the desired degree of oversizing. Fenestrated stent-grafts (Cook Europe, Bjaeverskov, Denmark) were constructed with a single 6-mm-wide fenestration at a distance of 21 mm from the fabric edge (Fig. 2B). The fenestrations were not reinforced. Since the study aimed to measure the proximal fixation strength only, all stent-grafts were truncated within the main body at 53 mm from the fabric edge, leaving the bare stent and the first 2 internal stents intact but removing the third external stent from the fabric graft (Fig. 2A). The actual contact length between both stent-graft types and the aorta was 36 mm.

All stent-grafts were crimped using a noose to introduce it into the aorta and deployed at the predetermined site under direct vision.

The fenestrated stent-graft was deployed to align the fenestration with the ostium of a selected side branch with an external diameter of ~5 mm. A 6-×20-mm balloon-expandable stent (Medtronic AVE, Santa Rose, CA, USA) was placed under direct vision through the fenestration into the side branch and deployed; the stent was then flared with a 12-mm angioplasty balloon.

Because of the natural taper of the bovine aorta, the vessel was reversed in the experiment so that the stent-graft was made to migrate from the narrow segment to the wide segment. Hence, the bare stent was oriented toward the narrower segment of aorta, which was sealed at the end using an internal plastic plug and external gasket arrangement. This plug contained a Luer connection for controlled pressurization of the aortic lumen and also a port to introduce a rigid endoscope for observing stent-graft behavior during the experiment. The caudal or unstented portion of the graft was connected to a 0.46-mm-diameter stainless steel wire with a 16-mm-diameter plastic plug, which was narrower than the aortic lumen to ensure that only the proximal portion of the stent-graft was in contact with the aorta. The wire was then brought to the exterior of the aorta through a hole in another plastic plug that sealed the end of the aorta toward the caudal end of the stent-graft. This hole contained an O-ring seal to allow free linear movement of the wire, while being leak-proof. The wire was connected to a digital force gauge (Model FG-5000; RS Components, Corby, UK) mounted securely on the moving stage of a manual linear drive operated by the turn of a wheel. Clockwise rotation of the wheel caused the stage to move to the left, thereby exerting a force on the stent-graft, which was continuously displayed on the force gauge. This gauge was equipped with a "peak-hold" facility to preserve the highest reading should a sudden drop occur in the force being measured. The force gauge was calibrated with known weights, and the maximum deviation was found to be ± 0.05 N.

Once the aorta was pressurized to the predetermined level, the linear drive was engaged, and any slack within the connecting wire was removed. A flag was placed on the wire to facilitate ready identification and measurement of any movement of the stent-graft. The handwheel was then rotated slowly while continuously recording the distraction force. The stent-graft behavior during this period was observed through the endoscope.

Each segment of aorta was used only once to avoid errors due to potential mechanical damage of the aorta during the experiment. Stent-grafts were reused only when free from deformation upon visual inspection, including the alignment of fixation barbs. Stent-grafts were reused only once to avoid potential errors due to metal fatigue and unidentified deformation. Results were grouped according to the degree of oversizing for standard and fenestrated stent-grafts. The data are presented as the mean ± standard deviation for each group. Two-way ANOVA with multiple comparisons (with Bonferroni correction) was used to compare groups.

RESULTS

With gradually increasing distraction force, the stent-graft migration was noted to occur in 2 distinct phases. There was an initial yield, corresponding to a displacement up to about 5 mm, which was attributed to embedding of the barbs into the aortic wall. Once this phase was complete, the stent-graft was able to resist migration for a period until a second yield occurred with increasing force, followed by movement of the stent-graft in relation to the aorta. The peak displacement forces (Table) corresponding to the 2 phases were described as initial displacement force (IDF) and final displacement force (FDF), respectively. For standard stent-grafts, the mean values of both IDF and FDF at 20% oversizing were significantly greater than the corresponding values at 10% oversizing ($p<0.001$), which in turn were greater than those at 5% oversizing ($p=0.02$). Results with fenestrated stent-grafts show a similar trend with the exception of a lack of significant difference between 20% and 10% oversizing levels ($p=0.054$). Both the initial and final displacement forces were significantly higher with fenestrated stent-grafts than with standard stent-grafts ($p<0.001$) at any degree of oversizing.

TABLE
Comparison of Initial Displacement Force (IDF) and Final Displacement Force (FDF) for 3 Oversizing Levels in Standard and Fenestrated Stent-Grafts

	5% Oversizing		10% Oversizing		20% Oversizing	
	IDF	FDF	IDF	FDF	IDF	FDF
Standard	3.39±0.37	8.10±0.92	4.32±0.63	10.76±1.74	7.69±1.18	16.82±0.92
Fenestrated	10.48±1.23	22.56±1.60	11.45±1.48	28.24±1.56	12.12±1.42	33.01±1.75

* $p<0.001$ for standard vs. fenestrated at each oversizing level.

The mean initial and final displacement forces in the standard and fenestrated stent-grafts for oversizing of 5%, 10%, and 20% are shown graphically in Fig. 3.

None of the experiments produced any macroscopic injury to the aortic wall after displacement. The only structural deformity noted within the stent-graft after forced displacement was upward distortion of the fixation barbs (Fig. 4). The AVE stents appeared compressed and bent after the experiments (Fig. 5).

DISCUSSION

Traditional stent-graft designs rely upon physical attributes of a deployed stent-graft, such as columnar strength and radial force, to maintain a durable fixation. Fixation appendages, such as hooks or barbs incorporated at attachment sites, and aortic neck length also increase fixation strength.[11–14] The main factors predisposing to late migration are late dilatation of the aneurysm neck, hemodynamic forces acting upon the stent-grafts, and mechanical disintegration of the device. Poor quality of the vessel at the proximal fixation zone and underutilization of the infrarenal neck at the time of graft deployment also reduce the fixation strength and predispose to migration.[15–18]

Fenestrated stent-grafts were introduced primarily to preserve renal or mesenteric branch vessel perfusion while recruiting the aortic wall at the level of these branches to provide proximal seal and fixation.[19,20] Stents are routinely placed from the aortic lumen into the visceral arteries through the fenestrations to enhance the fixation strength of the stent-graft.[21] However, migration of a fenestrated stent-graft could result in distortion of the visceral artery stent and consequent loss

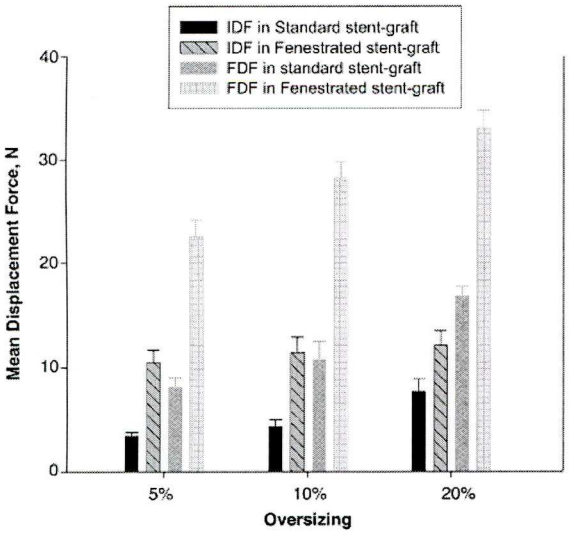

Figure 3 ◆ Graph showing the mean initial and final displacement forces in standard and fenestrated stent-grafts for oversizing of 5%, 10%, and 20%.

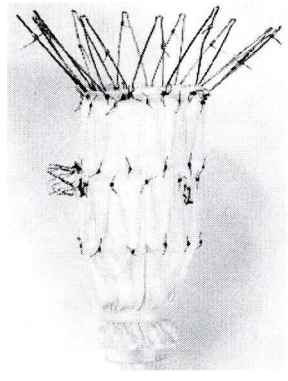

Figure 4 ◆ The only structural deformity noted within the stent-graft after forced displacement was upward distortion of the fixation barbs.

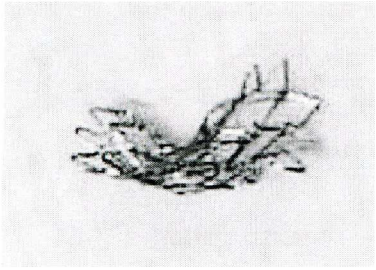

Figure 5 ◆ Appearance of the AVE stent after final displacement of the stent-graft.

of patency of this vessel in addition to the other consequences of migration. Although fixation strengths of standard stent-grafts have been reported,[11–14] there have been no reports relating to fenestrated stent-grafts. Furthermore, previous reports of fixation strength were based on experiments conducted on nonpressurized aortas, an important limitation to understanding the relationship between oversizing and fixation strength. As the experiments reported here were conducted with pressurized aortas, the results are likely to better represent the clinical situation.

An important observation of this study was the mode of migration of a stent-graft designed with fixation barbs. In the initial phase, a few millimeters of caudal migration, usually not exceeding the length of the barb (5 mm), occurred at a lower force as the barbs embedded into the aortic wall. More substantial force was required to cause subsequent migration in the second phase. The initial phase of migration is in accord with anecdotes from physicians familiar with similar stent-graft systems; they report that the stent-grafts may "settle" a few millimeters downwards after deployment. It is recognized that the Zenith stent-graft has a low incidence of migration, but we are unable to compare the fixation strength of different devices in our study since only one make of stent-graft was used.[22] The final displacement forces in standard stent-grafts varied from 8.1 to 16.8 N depending on the percentage oversizing. These values are smaller that those reported by Veerapen et al.[12] and Resch et al.[13] Although the former authors reported experiments with oversizing of 10% to 20%, Resch and colleagues did not provide this information.

The main difference with the present study is that the oversizing was accurately determined via known pressure-diameter relationships of the bovine aorta. It should be pointed out that the pressure per se did not have an influence on the displacement forces. The graft material was and remained porous to the saline during the experiments, and the pressure in the graft lumen was therefore similar to that in the aorta. Consequently, there was no net force acting on the graft due to the applied pressure.

The discovery of biphasic movement of this type of stent-graft upon application of a dislodging force raises some important issues. Full recruitment of the barbs into providing fixation strength appears to involve caudal movement of the stent-graft by a few millimeters as the barbs embed into the aortic wall. No such movement is caused deliberately in standard clinical practice. Should it occur naturally after deployment, the movement of a stent-graft by a few millimeters seldom causes significant problems with standard stent-grafts. It may, however, have significant implications for fenestrated stent-grafts. Since the barbs may not be fully engaged at the position of initial deployment, there is a risk of transferring some of the hemodynamic migratory forces to the interface between the stent-graft and the side-branch stent immediately after completion of aneurysm repair. Small-diameter stents that are suitable for side-branch placement are not designed to withstand the resultant asymmetric hoop stress. Failure or significant distortion of side-branch stents due to such stress can lead to loss of side-branch patency. A mechanism by which the initial phase of migration could be eliminated or made to occur in a controlled manner would have the potential to eliminate adverse effects. Moulding of the fixation areas using a conformable balloon may cause embedding of the barbs and eliminate the initial phase of migration or stent-graft settling.

Another important finding of this study was a relationship between oversizing and fixation strength; fixation strength increased with increasing oversizing up to 20%, which sup-

ports routine oversizing with self-expanding stent-grafts. In the case of fenestrated stent-grafts, however, the fixation strength did not increase significantly above 10% oversizing. This may be due to the fact that most of the fixation strength here was provided by the side-branch stent acting as an anchor rather than by the interaction between the stent-graft and the aortic wall.

Limitations

Although the methods of this study represent an enhancement compared to earlier in vitro studies of fixation strength,[11–14] there are a number of limitations to this study. The aortas used were straight tubular segments from healthy animals and as such cannot replicate some of the features of aneurysm anatomy, such as neck angulation, conical shape, or presence of calcification or thrombus. The applied distraction force was incremented gradually and thus may be functionally different from the repetitive forces that stent-grafts are subjected to in vivo.[23] Because of the natural taper of the aorta, the vessel was reversed in the experiment so that the stent-graft was made to migrate from the narrow to the wide segment, thereby potentially underestimating the fixation strength. Any error is likely to be small, but we considered that the alternative orientation was a worse option since this may potentially result in falsely high fixation strengths.

Although the length of the stent-graft used was 53 mm in both groups, only 36 mm of the covered section of the stent-graft was actually in contact with the aortic wall. This is at the upper end of the range of graft overlap with the aortic neck in vivo. The experiments were designed to measure the displacement force of the isolated proximal portion of the stent-graft, so truncated devices were used. We realize that the use of a complete bifurcated device may influence the measured forces, but the model used did not allow the effect to be investigated.

Conclusion

Our experiments demonstrated that proximal fixation strength of a self-expanding stent-graft with a proximal bare stent and barbs increased with increasing degree of oversizing up to 20% and that a fenestrated stent-graft configuration confers a greater proximal fixation than conventional devices. With such stent-graft design, full engagement of fixation barbs may cause movement of the stent-graft by a few millimeters before the full fixation strength of the device comes into action. This observation may have significant implications for fenestrated stent-graft design.

REFERENCES

1. Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet.* 2004;364:843–848.
2. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med.* 2004;351:1607–1618.
3. Alimi YS, Chakfe N, Rivoal E, et al. Rupture of an abdominal aortic aneurysm after endovascular graft placement and aneurysm size reduction. *J Vasc Surg.* 1998;28:178–183.
4. Torsello GB, Klenk E, Kasprzak B, et al. Rupture of abdominal aortic aneurysm previously treated by endovascular stent-graft. *J Vasc Surg.* 1998;28:184–187.
5. Lumsden AB, Allen RC, Chaikof EL, et al. Delayed rupture of aortic aneurysms following endovascular stent grafting. *Am J Surg.* 1995;170:174–178.
6. Liffman K, Lawrence-Brown MMD, Semmens JB, et al. Analytical modeling and numerical simulation of forces in an endoluminal graft. *J Endovasc Ther.* 2001;8:358–371.
7. Mohan IV, Harris PL, van Marrewijk CJ, et al. Factors and forces influencing stent-graft migration after endovascular aortic aneurysm repair. *J Endovasc Ther.* 2002;9:748–755.
8. Morris L, Delassus P, Walsh M, et al. A mathematical model to predict the in vivo pulsatile drag forces acting on bifurcated stent grafts used in endovascular treatment of abdominal aortic aneurysms (AAA). *J Biomech.* 2004;37:1087–1095.
9. Politz JK, Newman VS, Stewart MT. Late abdominal aortic aneurysm rupture after AneuRx repair: a report of three cases. *J Vasc Surg.* 2000;31:599–606.

10. Zarins CK, White RA, Fogarty TJ. Aneurysm rupture after endovascular repair using the AneuRx stent graft. *J Vasc Surg.* 2000;31:960–970.
11. Lambert AW, Williams DJ, Budd JS, et al. Experimental assessment of proximal stent-graft (Intervascular^{TM}) fixation in human cadaveric infrarenal aortas. *Eur J Vasc Endovasc Surg.* 1999;17:60–65.
12. Veerapen R, Dorandeu A, Serre I, et al. Improvement in proximal aortic endograft fixation: an experimental study using different stent-grafts in human cadaveric aortas. *J Endovasc Ther.* 2003;10:1101–1109.
13. Resch T, Malina M, Lindblad B, et al. The impact of stent design on proximal stent-graft fixation in the abdominal aorta: an experimental study. *Eur J Vasc Endovasc Surg.* 2000; 20:190–195.
14. Malina M, Lindblad B, Ivancev K, et al. Endovascular AAA exclusion: will stents with hooks and barbs prevent stent-graft migration? *J Endovasc Surg.* 1998;5:310–317.
15. Wolf YG, Hill BR, Lee WA, et al. Eccentric stent graft compression: an indicator of insecure proximal fixation of aortic stent graft. *J Vasc Surg.* 2001;33:481–487.
16. Sternbergh WC, Carter G, York JW, et al. Aortic neck angulation predicts adverse outcome with endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2002;35:482–486.
17. Matsumura JS, Moore WS. Clinical consequences of periprosthetic leak after endovascular repair of abdominal aortic aneurysm. *J Vasc Surg.* 1998;27:606–613.
18. Franko TJ, Zajko AB, Federle MP, et al. Endovascular repair of abdominal aortic aneurysm with the Ancure endograft: CT follow-up of perigraft flow and aneurysm size at 6 months. *J Vasc Interv Radiol.* 2000;11:429–435.
19. Anderson JL, Berce M, Hartley D. Endoluminal aortic grafting with renal and superior mesenteric artery incorporation by graft fenestration. *J Endovasc Ther.* 2001;8:3–15.
20. Browne TF, Hartley D, Purchas S, et al. A fenestrated covered suprarenal aortic stent. *Eur J Vasc Endovasc Surg.* 1999;18:445–449.
21. Verhoeven EL, Prins TR, Tielliu IF, et al. Treatment of short-necked infrarenal aortic aneurysms with fenestrated stent-grafts: short-term results. *Eur J Vasc Endovasc Surg.* 2004;27:477–483.
22. van Marrewijk CJ, Leurs LJ, Vallabhaneni SR, et al. Risk-adjusted outcome analysis of endovascular abdominal aortic aneurysm repair in a large population: how do stent-grafts compare? *J Endovasc Ther.* 2005;12:417–429.
23. Zarins CK, Bloch DA, Crabtree T, et al. Stent graft migration after endovascular aneurysm repair: importance of proximal fixation. *J Vasc Surg.* 2003;38:1264–1272.

Measurement of pulsatile haemodynamic forces in a model of a bifurcated stent graft for abdominal aortic aneurysm repair

S N Zhou[1,2], T V How[1]*, R A Black[1], S R Vallabhaneni[2], R McWilliams[3], and J A Brennan[2]
[1]Division of Clinical Engineering, School of Clinical Sciences, University of Liverpool, Liverpool, UK
[2]Regional Vascular Surgery Unit, Royal Liverpool University Hospital Trust, Liverpool, UK
[3]Department of Radiology, Royal Liverpool University Hospital Trust, Liverpool, UK

The manuscript was received on 9 March 2007 and was accepted after revision for publication on 18 December 2007.

DOI: 10.1243/09544119JEIM311

Abstract: The longitudinal haemodynamic force (LF) acting on a bifurcated stent graft for abdominal aortic aneurysm repair has been estimated previously using a simple one-dimensional analytical model based on the momentum equation which assumes steady flow of an inviscid fluid. Using an instrumented stent-graft model an experimental technique was developed to measure the LF under pulsatile flow conditions. The physical stent-graft model, with main trunk diameter of 30 mm and limb diameters of 12 mm, was fabricated from aluminium. Strain gauges were bonded on to the main trunk to determine the longitudinal strain which is related to the LF. After calibration, the model was placed in a pulsatile flow system with 40 per cent aqueous glycerol solution as the circulating fluid. The LF was determined using a Wheatstone bridge signal-conditioning circuit. The signals were averaged over 590 cardiac cycles and saved to a personal computer for subsequent processing. The LF was strongly dependent on the pressure but less so on the flowrate. The measured forces were higher than those predicted by the simplified mathematical model by about 6–18 per cent during the cardiac cycle. The excess measured forces are due to the viscous drag and the effect of pulsatile flow. The peak measured LF in this model of 30 mm diameter may exceed the fixation force of some current clinical endovascular stent grafts.

Keywords: migration, endovascular repair, strain gauges

1 INTRODUCTION

Abdominal aortic aneurysm (AAA) is a common vascular disorder which affects up to 5 per cent of the male population over 55 years of age in the West. Surgical replacement of the diseased aortic segment using a fabric graft has been the standard treatment of AAA. Endovascular repair (EVAR) using an endoluminal stent graft to exclude the AAA is an alternative that is finding wide acceptance throughout the world since it was first used clinically in the early 1990s [**1**]. Being minimally invasive, recovery of the patients is much quicker and obviates the need for cross-clamping of the aorta. The primary purpose of EVAR is to prevent death from aneurysm rupture. The aim of EVAR is to isolate the aneurysm from the aortic or systemic blood pressure while maintaining blood flow to the lower limbs. Clinical trials of EVAR show a significant improvement in 30 day mortality over conventional repair, which is maintained over the follow-up period of 4 years [**2**]. In the mid-term, however, a number of complications such as endoleak, distal migration of the device, thrombosis, and occlusion have been noted, necessitating regular surveillance of the patients. These complications represent significant causes of surgical re-interventions [**3**].

Pulsatile blood flow and pressure exert continual downward forces on the stent graft and the fixation

Corresponding author: Division of Clinical Engineering, School of Clinical Sciences, University of Liverpool, First Floor, Duncan Building, Daulby Street, Liverpool, L69 3GA, UK. email: thienhow@liverpool.ac.uk

means, such as the radial force, hooks, barbs, and the longitudinal columnar support of the device, are designed to resist these downward forces. Inadequate fixation or excessively high haemodynamic forces may cause distal migration and repressurization of the aneurysm sac, resulting eventally in rupture. Previous reports have shown that distal migration, defined as a longitudinal movement of at least 5 mm [**4**] or 10 mm [**5**], occurs in between 3 and 4 per cent of patients. The fixation strength of stent grafts has been estimated by measuring the longitudinal displacement force at the proximal fixation site of various commercially available stent grafts in a cadaveric model [**6**, **7**]. The median fixation strength ranged from 4.5 N to 26.6 N, compared with 150 N for the hand-sewn anastomosis in conventional repair.

In a previous study, one of the present authors and co-workers [**4**] showed that hypertension, aneurysm geometry, and iliac angulation, amongst other factors, were significantly associated with stent-graft migration [**4**]. These findings were validated using a simple one-dimensional analytical model based on a momentum equation, not accounting for the pulsatility of blood flow nor for the viscosity of the fluid. It was shown that under certain conditions, particularly in large stent grafts and in hypertension, the longitudinal force on a stent graft due to blood pressure and blood flow may exceed the fixation force causing stent-graft migration. The purpose of this study was to develop an experimental method to measure the longitudinal force (LF) in a model of a stent graft under pulsatile flow of a viscous fluid. A number of test runs were carried out to assess the feasibility of the technique and to compare the experimental data with the simplified analytical predictions.

2 THEORETICAL MODEL

A simple model of an idealized bifurcated device shown in Fig. 1 is considered to estimate the longitudinal force f_x exerted on the EVAR device. It is assumed that the bifurcation is planar and symmetrical and that the blood flow is distributed equally through two iliac limbs of equal diameter. The change in direction and velocity of flow due to the diameter change and the bifurcation angle causes a change in the momentum of the fluid. The momentum change and the pressure forces acting at the inlet and outlets result in a net longitudinal force f_x on the device which must be opposed to prevent its distal migration. It has been

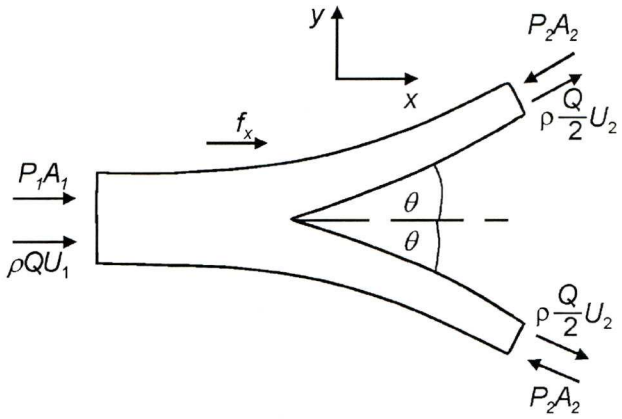

Fig. 1 Geometry and forces acting on a bifurcated stent graft

shown previously that f_x can be estimated by [**4**]

$$P_1A_1 - 2P_2A_2\cos\theta - f_x = \rho Q\left(\frac{U_2}{2}\cos\theta + \frac{U_2}{2}\cos\theta - U_1\right) \quad (1)$$

where P_1, A_1, and U_1 are the pressure, cross-sectional area, and velocity respectively at the inlet, P_2, A_2, and U_2 are the pressure, cross-sectional area, and velocity respectively at the outlet, ρ is the density of the fluid, and Q is the volume flowrate. The first two terms on the left-hand side of equation (1) represent the pressure forces at the inlet and outlets acting on areas A_1 and A_2 respectively. f_x is the axial component of the force exerted by the bifurcation on the fluid. The right-hand side of equation (1) represents the rate of increase in the axial component of momentum. Using the Bernoulli and continuity equations, expressions for P_2 and U_2 can be obtained in terms of P_1, U_1, A_1, and A_2, which are then substituted into equation (1) to give an equation for f_x as

$$f_x = P_1A_1 + \rho A_1U_1^2 - \rho\frac{A_1^2}{2A_2}U_1^2\cos\theta - 2A_2\cos\theta\left[P_1 + \rho\frac{U_1^2}{2}\left(1 - \frac{A_1^2}{4A_2^2}\right)\right] \quad (2)$$

f_x can be readily calculated for any device geometry and haemodynamic conditions using equation (2). In the transverse direction the pressure and momentum forces cancel out because of the symmetry and equal flow distribution and therefore $f_y = 0$.

3 MATERIALS AND METHOD

3.1 Measurement of the longitudinal force in an instrumented model of a bifurcated stent graft

The main body of the stent graft is subjected to the net LF f_x, which includes the pressure force in the main trunk and the iliac limbs, and the force due to the momentum change (Fig. 2). In this case, since a viscous fluid is used, f_x also includes the viscous drag force. The LF f_x will cause a longitudinal strain in the model which can be measured. In order to facilitate recording of the strain, the model is thinned locally as shown in Fig. 2, thereby increasing the strain level. The graft model is instrumented by means of strain gauges bonded on to the external surfaces of the thinned portion of the cylindrical segment. The instrumented stent-graft model was calibrated by applying a series of known weights to the model while monitoring the output from the strain gauge amplifier.

3.2 Stent-graft model

The model was machined from aluminium tubes joined with metal-loaded epoxy resin to form a bifurcation. The main trunk of internal diameter 30 mm and wall thickness 4 mm has a thinned segment 30 mm long and with a 0.1 mm wall thickness. The thinned segment was provided in order to increase the level of strains locally. Two strain gauges (CEA-13-250UN-350, Vishay Micro-Measurements, Reading, UK) from the same batch were bonded on to a thinned section using cyanoacrylate glue. They were placed parallel to the longitudinal axis of the main cylindrical section. As the model is fixed at its proximal end, the force f_x will result in a longitudinal strain that can be determined by means of the strain gauges. The strain gauges were connected in a half-bridge configuration and two 350 Ω high-stability precision resistors were used to complete the Wheatstone bridge (Fig. 2). The advantage over a single active strain gauge in a quarter-bridge configuration is greater sensitivity. However, the disadvantage for this half-bridge (and also the quarter-bridge configuration) is that the thermal effects do not cancel out and the output is therefore susceptible to temperature changes. To minimize self-heating of the strain gauges a low-voltage reference supply of 2.5 V (LM4140BCM-2.5, RS, Corby UK) was used. In addition, high-stability precision resistors (S350, 1 ppm/°C, Vishay Measurements Group UK, Basingstoke, UK) were used for the bridge completion resistors. Since the measurements could be affected by thermal zero drift, the signal output was monitored before and after each measurement. This was achieved by isolating the stent-graft model from any pressure load by closing the three ball valves at the inlet and outlets and opening the pressure port to atmosphere (see the flow circuit later in Fig. 3). Any drift was zeroed using the bridge balance. Provided that the strain gauge voltage supply and the instrumentation amplifier were switched on at least 2 h prior to the experiment to allow thermal equilibrium to be

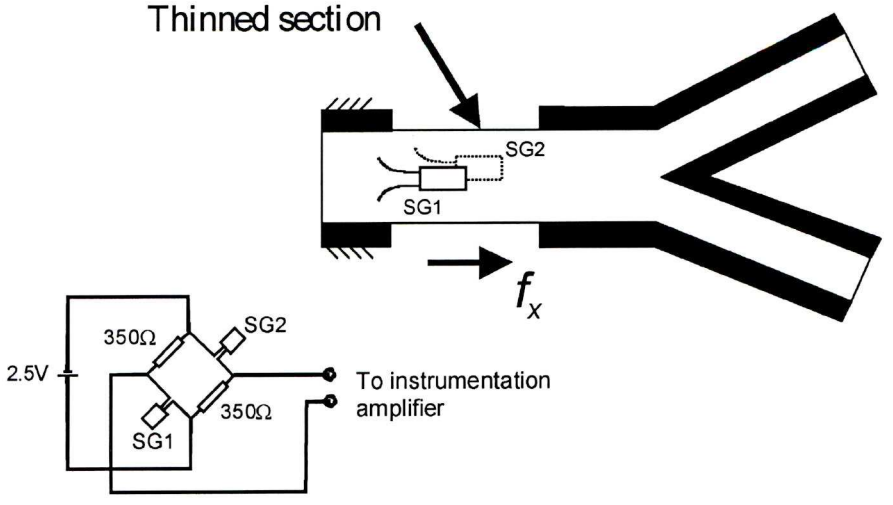

Fig. 2 Strain gauges bonded on to the thinned section of the stent-graft model. The proximal section of the model is fixed and the force f_x causes a longitudinal strain which can be measured by means of the strain gauges. The Wheatstone bridge circuit at the bottom shows the connection of the two active strain gauges and the fixed resistors

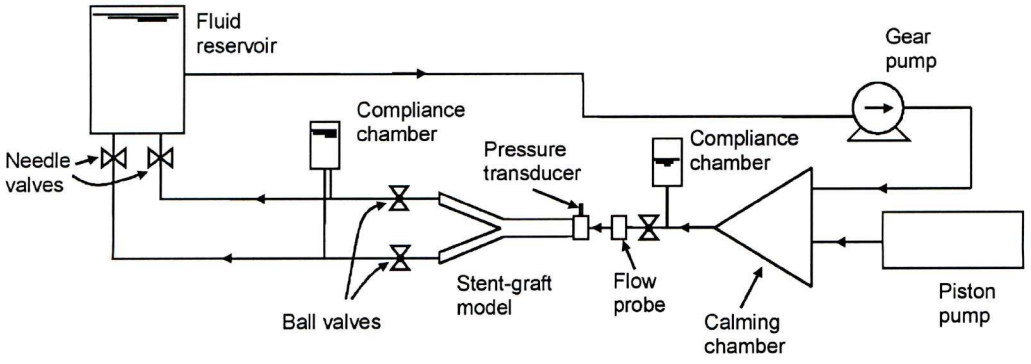

Fig. 3 Diagram of the flow circuit

reached, the zero drift over the duration of the experiment was found to be less than ± 5 mV (corresponding to ± 0.16 N).

3.3 Flow circuit

After calibration, as described above, the model was placed in a pulsatile flow circuit as shown in Fig. 3. Pulsatile flow with a waveform similar to that obtained in the abdominal aorta was generated by a custom-built servo-controlled piston pump and a gear pump (Micropump, Vancouver, Washington, USA). The circulating fluid was a 40 per cent aqueous solution of glycerol with dynamic viscosity similar to that of blood (a dynamic viscosity of 3.3×10^{-3} Pa s and a density of 1098 kg/m^3 at room temperature). An ultrasonic flow probe (24N, Transonic System Inc., Ithaca, New York, USA) was placed at the inlet pipe section to record the pulsatile flow. The pressure waveform just upstream of the aluminium model was also recorded using a pressure transducer (26PC, SensorTechnics UK, Rugby, UK). The pressure waveform was set to physiologically relevant values (diastolic pressure range, 60–90 mmHg; systolic pressure range, 130–160 mmHg) by adjusting the resistances of the needle valves and the volume of air in the proximal and distal compliance chambers. A long inlet length of approximately 2 m was placed between the calming chamber and the stent-graft model to ensure that laminar developed flow in the model. The strain gauge voltage supply and instrumentation amplifier were switched on at least 2 h prior to the experiment to allow the strain gauges to reach thermal equilibrium. The pressure, the flow, and the LF waveforms were each sampled at 100 samples/s and saved to a personal computer for subsequent analysis. To improve the signal-to-noise ratio, the data were recorded for 590 complete cycles and the average waveform was then determined.

4 RESULTS

Five experiments were carried out with the same flowrate of 1.5 l/min, the same heart rate of 60 beats per minute but different pressure waveforms. The average flow waveform, the average pressure waveform, and the net force f_x for a typical experiment are shown in Figs 4, 5, and 6 respectively. Each waveform was averaged over 590 cardiac cycles. Figure 6 shows the measured f_x waveform as well as the theoretical values calculated from equation (2) using the actual recorded pressure and flow waveforms. The measured force ranged from 3.4 N in diastole to 12.0 N at peak systole with an average value over the whole cycle of 5.5 N. The force and pressure waveforms appear to be almost in phase, indicating that pressure has a strong influence on the measured forces. It can be seen from Fig. 6 that the measured forces were greater than those calculated from equation (2). The difference between the measured and calculated forces expressed as a percentage of the measured values ranges from about 6 to 18 per cent of the measured values (Fig. 7).

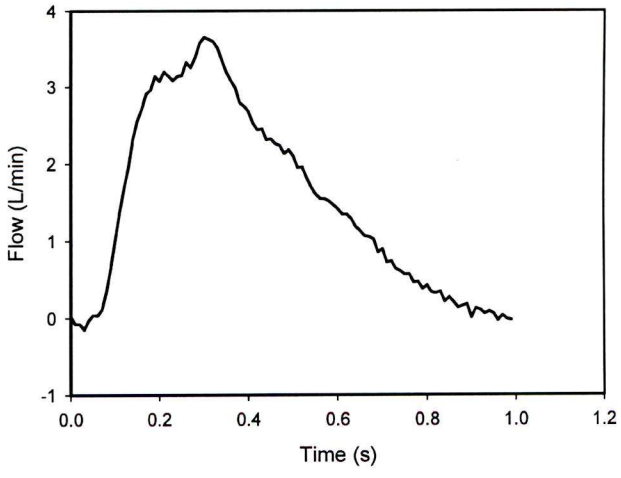

Fig. 4 Flow waveform

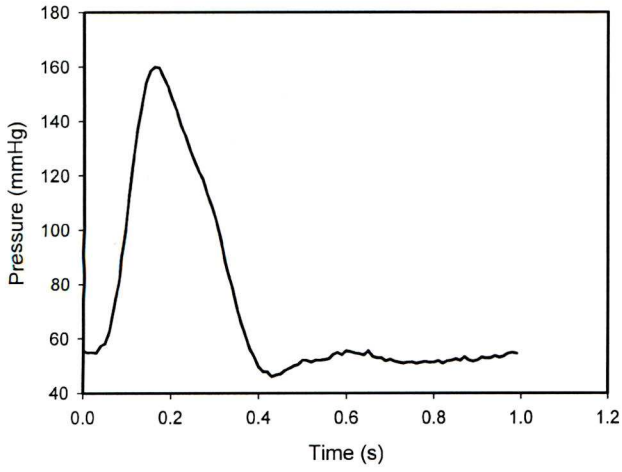

Fig. 5 Pressure waveform

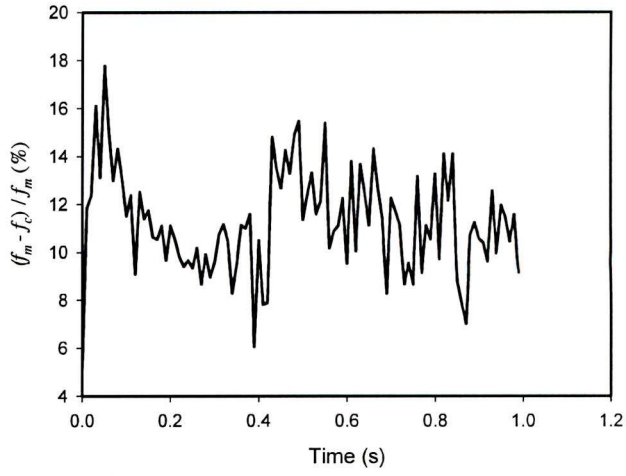

Fig. 7 Difference between the measured LF (f_m) and the calculated LF (f_c), expressed as a percentage of the measured value

5 DISCUSSION

One of the most important complications affecting the long-term success of EVAR of aortic aneurysms is stent-graft migration, i.e. movement of a stent graft relative to the vascular anatomy after complete deployment. Stent grafts depend upon a number of factors such as the radial force, the columnar strength, and the presence of hooks or barbs to remain stable in position since they are not sutured to the aortic wall and hence they are susceptible to migration. This has the potential to cause attachment-site endoleak and even a consequent aneurysm rupture [**3**, **4**, **8–10**]. A deployed stent graft constantly faces physiological forces that tend to cause stent-graft migration and therefore stent grafts should be designed to resist such migration. Measurements of the fixation strength of stent grafts indicate that commercial stent grafts can resist LFs up to 4.5–26.5 N depending on the design [**6**, **7**].

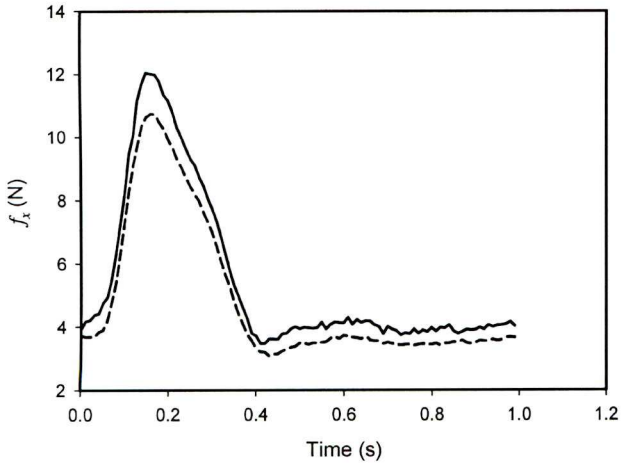

Fig. 6 Measured (solid curve) and calculated (dashed curve) LFs

The one-dimensional model (equation (2)) was derived using a number of simplifying assumptions about the fluid and the geometry of the bifurcation. Morris *et al.* [**11**], Li and Kleinstreuer [**12**], Kleinstreuer *et al.* [**13**], and Howell *et al.* [**14**] have carried out computational fluid dynamics studies of pulsatile flow in bifurcated devices and showed that the blood pressure had a strong influence on the haemodynamic forces acting on the stent graft. The contribution of blood flow velocity to these forces was relatively smaller than that of blood pressure. Li and Kleinstreuer [**12**] also found that the shape of the pressure waveform was a significant factor. Pressure waveforms with a high systolic slope produced higher LFs than those with lower systolic slopes. This was attributed to large flow accelerations which affected the forces acting on the device.

Using a gramometer, Volodos *et al.* [**15**] measured the LF in a tubular non-bifurcated stent graft subjected to a pulsatile flow of water. More recently, Sutalo *et al.* [**16**] developed an acrylic model of a bifurcated stent graft to measure LFs in a steady flow of water. The forces were measured by means of a load cell attached to the model and good agreement was found with the predictions of the simple one-dimensional model.

This study shows that the measured LF is in relatively good agreement with the simple one-dimensional steady inviscid model. Figure 7 shows the difference expressed as a percentage of the measured values. It can be seen that the maximum difference occurs during the midsystolic phase of the

pressure waveform. To obtain an estimate of the influence of the viscosity of the fluid and the pulsatility of the flow, first the pressure forces are evaluated from the first two terms of equation (1), i.e., $P_1A_1 - 2P_2A_2 \cos\theta$. (Using the Bernouilli and continuity equations, it can be shown that $2P_2A_2\cos\theta = 2A_2\cos\theta\{P_1+\rho(U_1^2/2)[1-A_1^2/(4A_2^2)]\}$. This is then subtracted from the measured LF and the results are shown in Fig. 8. The fluid viscosity and pulsatility of the flow therefore contributes approximately 0.2–1.2 N to the measured LF which ranged from about 4 to 12 N.

There are several limitations to this study. First, the model stent graft was fabricated from aluminium and therefore the compliance of the actual stent graft was not replicated. However, the basic geometry of a typical aortic stent graft is replicated in terms of the dimensions of the main trunk and the iliac limbs and the angle of bifurcation. In patients, the stent graft must conform to the anatomy of the aneurysmal aorta which in the majority of cases is complex with various degrees of non-uniformity. The forces in an actual stent graft in a patient may therefore be different and will depend on its geometrical configuration in the aneurysm. Second, the luminal surface of the model was smooth while the blood-contacting surface of the graft is rough. The dimensions of the roughness are determined by the size of the yarn used in fabricating the fabric graft, which is usually of a woven construction. The diameter of the yarn is typically of the order of 0.1 mm [**17**]. The surface roughness will have an influence on the resistance to flow and will therefore contribute to the LF on the stent graft. Within a relatively short period after surgery, however, a thin layer of thrombus will form on the luminal surface of the fabric and this will be transformed into a smooth organized fibrin which is firmly supported by the fabric structure [**17**]. Finally, the highly simplified one-dimensional inviscid model can provide only rough estimates of the forces to which a stent graft is subjected. Nevertheless, this model is still useful in providing acceptable estimates, as shown by reports based on computational fluid dynamics studies [**11–14**].

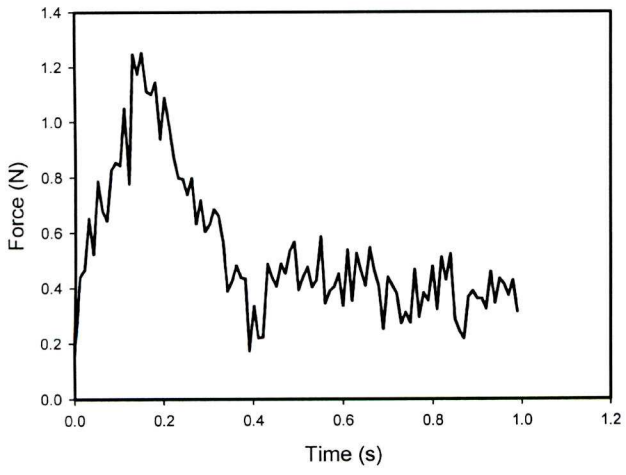

Fig. 8 LF due to viscous drag and pulsatility

In conclusion, the LF acting on a stent graft can be determined experimentally using an instrumented device. The LF is strongly dependent on the pressure. The fluid viscosity and pulsatility contribute between 6 and 18 per cent of the total LF. *In vivo*, however, these values may be different because of the compliance, the surface roughness of the actual stent graft, and the complex anatomy of the aortic aneurysm. These results indicate that, under certain conditions, the LF can exceed the fixation force of some of the current endovascular stent grafts and may therefore lead to the distal migration and its potentially serious consequences.

REFERENCES

1 **Parodi, J. C., Palmaz, J. C.,** and **Barone, H. D.** Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann. Vascular Surg.*, 1991, **5**, 491–499.

2 EVAR trial participants, Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet*, 2005, **365**, 2179–2186.

3 **Harris, P. L., Vallabheneni, S. R., Desgranges, P., Becquemin, J. P., Van Marriewijk, C.,** and **Laheij, R. J.** Incidence and risk factors of late rupture, conversion, and death after endovascular repair of infrarenal aortic aneurysms: the EUROSTAR experience. *J. Vascular Surg.*, 2000, **32**, 739–749.

4 **Mohan, I. V., Harris, P. L., Van Marriewijk, C., Laheij, R. J. F.,** and **How, T. V.** Factors and forces influencing stent-graft migration after endovascular aortic aneurysm repair. *J. Endovascular Therapy*, 2002, **9**, 748–755.

5 **Greenberg, R. K., Turc, A., Haulon, S., Srivastava, S. D., Sarac, T. P., O'Hara, P. J., Lyden, S. P.,** and **Ouriel, K.** Stent-graft migration: a reappraisal of analysis methods and proposed revised definition. *J. Endovascular Therapy*, 2004, **11**, 353–363.

6 **Resch, T., Ivancev, K., Brunkwall, J., Nyman, U., Malina, M.,** and **Lindblad, B.** Distal migration of stent-grafts after endovascular repair of abdominal aortic aneurysms. *J. Vascular Interventional Radiology*, 1999, **10**, 257–264.

7 **Veerapen, R., Dorandeu, A., Serre, I., Berthet, J. P., Marty-Ane, C. H., Mary, H.,** and **Alric, P.** Improvement in proximal aortic endograft fixation: an experimental study using different stent-grafts in human cadaveric aortas. *J. Endovascular Therapy*, 2003, **10**, 1101–1109.

8 **Alimi, Y. S., Chakfe, N., Rivoal, E., Slimane, K. K., Valerio, N., Riepe, G., Kretz, J. G.,** and **Juhan, C.** Rupture of an abdominal aortic aneurysm after endovascular graft placement and aneurysm size reduction. *J. Vascular Surg.*, 1998, **28**, 178–183.

9 **Torsello, G. B., Klenk, E., Kasprzak, B.,** and **Umscheid, T.** Rupture of abdominal aortic aneurysm previously treated by endovascular stent graft. *J. Vascular Surg.*, 1998, **28**, 184–187.

10 **Lumsden, A. B., Allen, R. C., Chaikoff, E. L., Resnikoff, M., Moritz, M. W., Gerhard, H.,** and **Castronuovo, J. J.** Delayed rupture of aortic aneurysms following endovascular stent grafting. *Am. J. Surg.*, 1995, **170**, 174–178.

11 **Morris, L., Delassus, P., Walsh, M.,** and **McGloughlin, T.** A mathematical model to predict the in vivo pulsatile drag forces acting on bifurcated stent grafts used in endovascular treatment of abdominal aortic aneurysms (AAA). *J. Biomechanics*, 2004, **37**, 1087–1095.

12 **Li, Z.** and **Kleinstreuer, C.** Analysis of biomechanical factors affecting stent-graft migration in an abdominal aortic aneurysm model. *J. Biomechanics*, 2006, **39**, 2264–2273.

13 **Kleinstreuer, C., Li, Z.,** and **Farber, M. A.** Fluid–structure interaction analyses of stented abdominal aortic aneurysms. *A. Rev. Biomed. Engng*, 2007, **9**, 169–204.

14 **Howell, B. A., Kim, T., Cheer, A., Dwyer, H., Saloner, D.,** and **Chuter, T. A. M.** Computational fluid dynamics within bifurcated abdominal aortic stent-grafts. *J. Endovascular Therapy*, 2007, **14**, 138–143.

15 **Volodos, S. M., Sayers, R. D., Gostelow, J. P.,** and **Bell, P.** Factors affecting the displacement force exerted on a stent graft after AAA repair – an *in vitro* study. *Eur. J. Vascular Endovascular Surg.*, 2003, **26**, 596–601.

16 **Sutalo, I. D., Liffman, K., Lawrence-Brown, M. M. D.,** and **Semmens, J. B.** Experimental force measurements on a bifurcated endoluminal stent graft model: comparison with theory. *Vascular*, 2005, **13**, 98–106.

17 **How, T. V., Guidoin, R.,** and **Young, S. K.** Engineering design of vascular prostheses. *Proc. Instn Mech. Engrs, Part H: J. Engineering in Medicine*, 1992, **206**, 61–71.

PRESENTATIONS IN NATIONAL AND INTERNATIONAL SCIENTIFIC MEETINGS FROM THIS RESEARCH PROJECT

1: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris.

Greater "oversizing" of aortic endografts is required for shorter aneurysm necks in endovascular aortic aneurysm repair (EVAR).

Oral presentation in 14th International Society of Endovascular Specialist Congress, Phoenix, Arizona. USA. 12-16 Feb 2006.

2: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

Measurement of Longitudinal Haemodynamic Force on Bifurcated Endograft Model

Oral presentation in International Conference of Endovascology-2005, Shanghai, China. 1-4 Dec 2005.

3: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

Investigation of the effectiveness of proximal seal in fenestrated endograft for endovascular aortic aneurysm repair (EVAR).

Oral presentation in International Conference of Endovascology-2005, Shanghai, China. 1-4 Dec 2005.

4: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

How secure is the proximal seal in fenestrated endovascular aortic aneurysm repair?

Oral presentation in 14th Annual Conference of ASGBI. Edinburgh 3-5 May 2006.

5: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

Longitudinal haemodynamic force acting on bifurcated endograft model is greater than previously estimated.

Poster presentation in 14th Annual Conference of ASGBI. Edinburgh 3-5 May 2006.

6: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

Comparison of the fixation strength of fenestrated and non-fenestrated stent-grafts for Endovascular abdominal aortic aneurysm repair (EVAR).

Oral presentation in Annual Meeting of Vascular Society of Great Britain and Ireland. Bournemouth International Centre, Bournemouth, UK. 23-25 Nov 2005.

7: S S N Zhou, J Brennan, R McWilliams, T V How, S R Vallabhaneni, G L Gilling-Smith, P L Harris

Greater "oversizing" of aortic endografts is required for shorter aneurysm necks in endovascular aortic aneurysm repair (EVAR).

Oral in Annual Meeting of Vascular Society of Great Britain and Ireland. Bournemouth International Centre, Bournemouth, UK. 23-25 Nov 2005.

8: S S N Zhou, J Brennan, R McWilliams, T V How, G L Gilling-Smith, P L Harris

EVAR: The Effect of hooks and oversizing on the strength of proximal fixation of the stent-graft.

Oral in SARS (Society of Academic and Research Surgery) Annual conference, Newcastle, UK. 12-14 January 2005.